

Set Items Description

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Ref	Items	Index-term
E1	53	AU=FI SCHER, G W
E2	24	AU=FI SCHER, G*
E3	0	*AU=FI SCHER, G?
E4	3	AU=FI SCHER, GA
E5	11	AU=FI SCHER, GABOR
E6	5	AU=FI SCHER, GABOR M
E7	4	AU=FI SCHER, GABRI EL
E8	10	AU=FI SCHER, GABRI ELA
E9	1	AU=FI SCHER, GABRI ELA A
E10	3	AU=FI SCHER, GABRI ELA A.
E11	57	AU=FI SCHER, GABRI ELE
E12	17	AU=FI SCHER, GABRI ELLA

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Ref	Items	Index-term
E13	2	AU=FI SCHER, GABY
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E16	3	AU=FI SCHER, GARY J.
E17	4	AU=FI SCHER, GARY JOHN
E18	1	AU=FI SCHER, GARY R
E19	2	AU=FI SCHER, GARY R.
E20	1	AU=FI SCHER, GARY S
E21	3	AU=FI SCHER, GARY S.
E22	4	AU=FI SCHER, GARY W
E23	16	AU=FI SCHER, GARY W
E24	1	AU=FI SCHER, GARY WALTER

Enter P or PAGE for more

? e au=fischer, ge?

Ref	Items	Index-term
E1	2	AU=FI SCHER, GC.
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E5	14	AU=FI SCHER, GENA
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E8	64	AU=FI SCHER, GEORG
E9	5	AU=FI SCHER, GEORG M
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E11	5	AU=FI SCHER, GEORGE A
E12	17	AU=FI SCHER, GEORGE A.

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Ref	Items	Index-term
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E14	1	AU=FI SCHER, GEORGE FREDERICK
E15	1	AU=FI SCHER, GEORGE H.
E16	2	AU=FI SCHER, GEORGE J
E17	7	AU=FI SCHER, GEORGE J.
E18	2	AU=FI SCHER, GEORGE L

E19	14	AU=FI SCHER,	GEORGE L.
E20	2	AU=FI SCHER,	GEORGE LUDW G
E21	1	AU=FI SCHER,	GEORGE T., II
E22	1	AU=FI SCHER,	GEORGE TEHAN
E23	2	AU=FI SCHER,	GEORGE W
E24	1	AU=FI SCHER,	GEORGE W

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Ref	Items	Index-term
E25	6	AU=FI SCHER, GEORGES
E26	61	AU=FI SCHER, GERALD
E27	1	AU=FI SCHER, GERALD CHARLES
E28	2	AU=FI SCHER, GERALD R
E29	7	AU=FI SCHER, GERALD W
E30	25	AU=FI SCHER, GERALD W
E31	3	AU=FI SCHER, GERALD WALTER
E32	2	AU=FI SCHER, GERARD
E33	496	AU=FI SCHER, GERD
E34	2	AU=FI SCHER, GERD M
E35	8	AU=FI SCHER, GERD M
E36	1	AU=FI SCHER, GERD.

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61	AU=FI SCHER,	GERALD
1	AU=FI SCHER,	GERALD CHARLES
2	AU=FI SCHER,	GERALD R
7	AU=FI SCHER,	GERALD W
25	AU=FI SCHER,	GERALD W
3	AU=FI SCHER,	GERALD WALTER
99	E26- E31	

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? rd

>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S2 88 RD (unique items)

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Processed 10 of 56 files ...

Processed 20 of 56 files ...

Processed 30 of 56 files ...

Processed 40 of 56 files ...

Processed 50 of 56 files ...

Completed processing all files

88 S2

0 ?TECHOIC?

S3 0 S2 AND ?TECHOIC?

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PLEASE ENTER A COMMAND OR BE LOGGED OFF IN 5 MINUTES

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Ref	Items	Index-term
E1	53	AU=FI SCHER, G W
E2	24	AU=FI SCHER, G*
E3	0	*AU=FI SCHER, G?
E4	3	AU=FI SCHER, GA
E5	11	AU=FI SCHER, GABOR
E6	5	AU=FI SCHER, GABOR M
E7	4	AU=FI SCHER, GABRI EL

E8	10	AU=FI SCHER,	GABRI ELA
E9	1	AU=FI SCHER,	GABRI ELA A
E10	3	AU=FI SCHER,	GABRI ELA A.
E11	57	AU=FI SCHER,	GABRI ELE
E12	17	AU=FI SCHER,	GABRI ELLA

Enter P or PAGE for more
 ? e au=fischer, gerald

Ref	Items	Index-term
E1	1	AU=FI SCHER, GEORGE W
E2	6	AU=FI SCHER, GEORGES
E3	61 *	AU=FI SCHER, GERALD
E4	1	AU=FI SCHER, GERALD CHARLES
E5	2	AU=FI SCHER, GERALD R
E6	7	AU=FI SCHER, GERALD W
E7	25	AU=FI SCHER, GERALD W
E8	3	AU=FI SCHER, GERALD WALTER
E9	2	AU=FI SCHER, GERARD
E10	496	AU=FI SCHER, GERD
E11	2	AU=FI SCHER, GERD M
E12	8	AU=FI SCHER, GERD M

Enter P or PAGE for more
 ? s e3-e8

	61	AU=FI SCHER, GERALD
	1	AU=FI SCHER, GERALD CHARLES
	2	AU=FI SCHER, GERALD R
	7	AU=FI SCHER, GERALD W
	25	AU=FI SCHER, GERALD W
	3	AU=FI SCHER, GERALD WALTER
S4	99	E3- E8
? s s4 and (lipotechoic or techoic)		
	99	S4
	196	LI POTECHOI C
	346	TECHOI C
S5	0	S4 AND (LI POTECHOI C OR TECHOI C)
? s s4 and (lipoteichoic or teichoic)		
	99	S4
	14841	LI POTEI CHOI C
	13613	TEI CHOI C
S6	8	S4 AND (LI POTEI CHOI C OR TEI CHOI C)
? rd		

>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S7 6 RD (unique items)

? t s7/3, k/1-6

>>>KW C option is not available in file(s): 399

7/3, K/1 (Item 1 from file: 24)
 DIALOG(R) File 24: CSA Life Sciences Abstracts
 (c) 2010 CSA. All rts. reserv.

0003697420 IP ACCESSI ON NO: 9200024
 Safety and pharmacokinetics of a chimerized anti-lipoteichoic acid
 monoclonal antibody in healthy adults

Weisman, Leonard E; Fischer, Gerald W; Thackray, Helen M; Johnson,
 Karen E; Schuman, Richard F; Mandy, George T; Stratton, Beth E; Adams,
 Page 3

10601171monoclonal.txt

Karen M. Kramer, William G. Mond, James J.
Department of Pediatrics, Baylor College of Medicine, Houston, TX, United
States, [mailto:lweisman@bcm.edu]

International Immunopharmacology, v 9, n 5, p 639-644, May 2009
PUBLICATION DATE: 2009

PUBLISHER: Elsevier Science, P. O. Box 211 Amsterdam 1000 AE Netherlands,
[mailto:nlinfo-f@elsevier.nl], [URL: http://www.elsevier.nl/]

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 1567-5769
FILE SEGMENT: Immunology Abstracts

Safety and pharmacokinetics of a chimerized anti-lipoteichoic acid
monoclonal antibody in healthy adults

Weisman, Leonard E; Fischer, Gerald W; Thackray, Helen M; Johnson,
Karen E; Schuman, Richard F; Mandy, George T; Stratton...

ABSTRACT:

A chimerized (murine/human) monoclonal antibody (pagibaximab) against
lipoteichoic acid (LTA) and protective in animal models for
coagulase-negative staphylococci (CONS) and Staphylococcus aureus...

DESCRIPTORS: Animal models; Bacteremia; Clinical isolates; Clinical
trials; Data processing; Drugs; Immunoglobulin G; Infection;
Intravenous administration; Lipoteichoic acid; Monoclonal
antibodies; Pharmacokinetics; Risk groups; Statistical analysis;
Staphylococcus aureus; Staphylococcus epidermidis

7/3, K/2 (Item 2 from file: 24)
DIALOG(R) File 24: CSA Life Sciences Abstracts
(c) 2010 CSA. All rights reserved.

0002808824 IP ACCESSION NO: 6495019
Opsonic and protective monoclonal and chimeric antibodies specific for
lipoteichoic acid of gram positive bacteria

Fischer, Gerald W; Schuman, Richard F; Wong, Hing; Stinson,
Jeffrey R

, September 6, 2005
PUBLICATION DATE: 2005

DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
FILE SEGMENT: Medical & Pharmaceutical Biotechnology Abstracts

Opsonic and protective monoclonal and chimeric antibodies specific for
lipoteichoic acid of gram positive bacteria

Fischer, Gerald W; Schuman, Richard F; Wong, Hing; Stinson,
Jeffrey R

ABSTRACT:

The present invention encompasses monoclonal and chimeric antibodies that bind to lipoteichoic acid of Gram positive bacteria. The antibodies also bind to whole bacteria and enhance phagocytosis...

...unknown means to diagnose, prevent and/or treat infections caused by gram positive bacteria bearing lipoteichoic acid. This invention also encompasses a peptide mimic of the lipoteichoic acid epitope binding site defined by the monoclonal antibody. This epitope or epitope peptide mimic identifies other antibodies that may bind to the lipoteichoic acid epitope. Moreover, the epitope or epitope peptide mimic provides a valuable substrate for the...

DESCRIPTORS: Gram positive bacteria; Epitopes; Lipoteichoic acid; Monoclonal antibodies; Infection; Vaccines; Phagocytosis; Patients

7/3, K/3 (Item 1 from file: 399)

DI ALOG(R) File 399: CA SEARCH(R)

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151099228 CA: 151(5)99228b JOURNAL

Phase 1/2 double-blind, placebo-controlled, dose escalation, safety, and pharmacokinetic study of pagibaximab (BSYX-A110), an antistaphylococcal monoclonal antibody for the prevention of staphylococcal bloodstream infections, in very-low-birth-weight neonates

AUTHOR(S): Weisman, Leonard E.; Thackray, Helen M.; Garcia-Prats, Joseph A.; Nesin, Mirjana; Schneider, Joseph H.; Fretz, Jennifer; Kokai-Kun, John F.; Mond, James J.; Kramer, William G.; Fischer, Gerald W

LOCATION: Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA

JOURNAL: Antimicrob. Agents Chemother. (Antimicrobial Agents and Chemotherapy) DATE: 2009 VOLUME: 53 NUMBER: 7 PAGES: 2879-2886 CODEN: AMACQ ISSN: 0066-4804 LANGUAGE: English PUBLISHER: American Society for Microbiology

7/3, K/4 (Item 2 from file: 399)

DI ALOG(R) File 399: CA SEARCH(R)

(c) 2010 American Chemical Society. All rights reserved.

144348884 CA: 144(19)348884r PATENT

Effective immunogenic compositions comprising combinations of staphylococcal antigens and capsular polysaccharides

INVENTOR(AUTHOR): Castado, Gindy; Fischer, Gerald Walter; Foster, Simon James; Kokai-Kun, John Fitzgerald; Lecrenier, Nicolas Pierre Fernand; Lees, Andrew; Mond, James Jacob; Neyt, Cecile Anne; Poolman, Jan

LOCATION: Belg.

ASSIGNEE: GlaxoSmithKline Biologicals S.A.; The University of Sheffield; Biosynexus Incorporated

PATENT: PCT International ; WO 200632475 A2 DATE: 20060330

APPLICATION: WO 2005EP10199 (20050920) *GB 200421079 (20040922) *GB 200421078 (20040922) *GB 200421081 (20040922) *GB 200421082 (20040922) *GB 20053143 (20050215)

PAGES: 136 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: A61K-000/A

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BW; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; EG; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KM; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; LY; MA; MD; MG; MK; MN; MW; MX; MY; NA; NG; NI; NO; NZ; OM; PG; PH; PL; PT; RO; RU; SC; SD; SE; SG; SK; SL; SM; SY; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM DESIGNATED REGIONAL: AT; BE; BG; CH

10601171monoclonal.txt

; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IS; IT; LT; LU; LV; MC;
NL; PL; PT; RO; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML;
MR; NE; SN; TD; TG; BW; GH; GM; KE; LS; MW; MZ; NA; SD; SL; SZ; TZ; UG; ZM;
ZW AM; AZ; BY; KG; KZ; MD; RU; TJ; TM

7/3, K/5 (Item 3 from file: 399)

DI ALOG(R) File 399: CA SEARCH(R)

(c) 2010 American Chemical Society. All rts. reserv.

140058441 CA: 140(5)58441v PATENT

Opsonic monoclonal and chimeric antibodies specific to lipoteichoic acid
of Gram positive bacteria for diagnosis and treatment of infection

INVENTOR(AUTHOR): Stinson, Jeffrey R.; Schuman, Richard F.; Mond, James
J.; Lees, Andrew; Fischer, Gerald Walter

LOCATION: USA

PATENT: U.S. Pat. Appl. Publ.; US 20030235578 A1 DATE: 20031225

APPLICATION: US 323927 (20021220) *US 97055 (19980615) *US PV343503
(20011221)

PAGES: 42 pp., Cont.-in-part of U.S. 6,610,293. CODEN: USXXOO

LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: 424130100; A61K-039/395A; C07K-016/18B

7/3, K/6 (Item 4 from file: 399)

DI ALOG(R) File 399: CA SEARCH(R)

(c) 2010 American Chemical Society. All rts. reserv.

139116277 CA: 139(8)116277p PATENT

Opsonic monoclonal and chimeric antibodies specific for lipoteichoic acid
of Gram positive bacteria

INVENTOR(AUTHOR): Stinson, Jeffrey R.; Schuman, Richard F.; Mond, James
J.; Lees, Andrew; Fischer, Gerald Walter

LOCATION: USA

ASSIGNEE: Biosynexus Incorporated

PATENT: PCT International; WO 200359260 A2 DATE: 20030724

APPLICATION: WO 2002US41033 (20021223) *US PV343503 (20011221)

PAGES: 99 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: A61K-000/A

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;
CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH;
GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU;
LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SC; SD;
SE; SG; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM;
ZW AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS
; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW AT; BE; BG; CH; CY; CZ; DE; DK; EE;
ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; SI; SK; TR; BF; BJ; CF; CG;
CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG
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Ref	Items	Index-term
E1	5	AU=WONG, HI N- YONG
E2	1	AU=WONG, HI N- YOUNG
E3	43	* AU=WONG, HI NG
E4	44	AU=WONG, HI NG C
E5	69	AU=WONG, HI NG C.
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E10	1	AU=WONG, HI NG KWOK

E11 7 AU=WONG, HI NG LOK
 E12 2 AU=WONG, HI NG NAM I VY

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43 AU=WONG, HI NG
 44 AU=WONG, HI NG C
 69 AU=WONG, HI NG C.
 3 AU=WONG, HI NG C*
 1 AU=WONG, HI NG CHEUG
 13 AU=WONG, HI NG CHEUNG
 1 AU=WONG, HI NG KA
 1 AU=WONG, HI NG KWOK
 7 AU=WONG, HI NG LOK
 2 AU=WONG, HI NG NAM I VY

S8 184 E3-E12

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184 S8
 14841 LI POTEI CHOI C
 13613 TEI CHOI C

S9 3 S8 AND (LI POTEI CHOI C OR TEI CHOI C)

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>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S10 2 RD (unique items)

? t s10/3,k/1-2

>>>KW C option is not available in file(s): 399

10/3, K/1 (Item 1 from file: 24)
 DIALOG(R) File 24: CSA Life Sciences Abstracts
 (c) 2010 CSA. All rts. reserv.

0002808824 IP ACCESSION NO: 6495019
 Opsonic and protective monoclonal and chimeric antibodies specific for
 lipoteichoic acid of gram positive bacteria

Fischer, Gerald W Schuman, Richard F; Wong, Hing; Stinson,
 Jeffrey R

, September 6, 2005
 PUBLICATION DATE: 2005

DOCUMENT TYPE: Patent
 RECORD TYPE: Abstract
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 FILE SEGMENT: Medical & Pharmaceutical Biotechnology Abstracts

Opsonic and protective monoclonal and chimeric antibodies specific for
 lipoteichoic acid of gram positive bacteria

Fischer, Gerald W Schuman, Richard F; Wong, Hing; Stinson,
 Jeffrey R

ABSTRACT:

The present invention encompasses monoclonal and chimeric antibodies that
 bind to lipoteichoic acid of Gram positive bacteria. The antibodies
 also bind to whole bacteria and enhance phagocytosis...

...unknown means to diagnose, prevent and/or treat infections caused by gram positive bacteria bearing lipoteichoic acid. This invention also encompasses a peptide mimic of the lipoteichoic acid epitope binding site defined by the monoclonal antibody. This epitope or epitope peptide mimic identifies other antibodies that may bind to the lipoteichoic acid epitope. Moreover, the epitope or epitope peptide mimic provides a valuable substrate for the...

DESCRIPTORS: Gram positive bacteria; Epitopes; Lipoteichoic acid;
Monoclonal antibodies; Infection; Vaccines; Phagocytosis; Patients

10/3, K/2 (Item 1 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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139306536 CA: 139(20)306536v PATENT

Production of humanized antibodies by optimizing individual framework regions for diagnostic and therapeutic uses

INVENTOR(AUTHOR): Wong, Hing C.; Stinson, Jeffrey R.; Mosquera, Luis A.

LOCATION: USA

ASSIGNEE: Sunol Molecular Corporation

PATENT: U.S. Pat. Appl. Publ.; US 20030190705 A1 DATE: 20031009

APPLICATION: US 230880 (20020829) *US PV343306 (20011029) *US 990586 (20011121)

PAGES: 95 pp., Cont.-in-part of U.S. Pat. Appl. 2003 109,680. CODEN:

USXXCO LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: 435069100; C12P-021/02A; C12N-005/06B; C07K-016/44B;

C07H-021/04B

? e au=schuman, richard

Ref	Items	Index-term
E1	1	AU=SCHUMAN, RALPH HENRY
E2	2	AU=SCHUMAN, RF
E3	7	*AU=SCHUMAN, RI CHARD
E4	1	AU=SCHUMAN, RI CHARD C.
E5	5	AU=SCHUMAN, RI CHARD F
E6	16	AU=SCHUMAN, RI CHARD F.
E7	1	AU=SCHUMAN, RI CHARD FARREL
E8	7	AU=SCHUMAN, RI CHARD J
E9	1	AU=SCHUMAN, RI CHARD M
E10	3	AU=SCHUMAN, RI CK
E11	1	AU=SCHUMAN, ROBERT
E12	1	AU=SCHUMAN, ROBERT A.

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7	AU=SCHUMAN, RI CHARD
1	AU=SCHUMAN, RI CHARD C.
5	AU=SCHUMAN, RI CHARD F
16	AU=SCHUMAN, RI CHARD F.
1	AU=SCHUMAN, RI CHARD FARREL
7	AU=SCHUMAN, RI CHARD J
1	AU=SCHUMAN, RI CHARD M
S11	38 E3-E9

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13613	TEICHOIC

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S12 6 S11 AND (LIPOTEICHOIC OR TEICHOIC)
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>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S13 4 RD (unique items)
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>>>KWC option is not available in file(s): 399

13/3,K/1 (Item 1 from file: 24)
DIALOG(R) File 24: CSA Life Sciences Abstracts
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0003697420 IP ACCESSION NO: 9200024
Safety and pharmacokinetics of a chimerized anti-lipoteichoic acid
monoclonal antibody in healthy adults

Weisman, Leonard E; Fischer, Gerald W; Thackray, Helen M; Johnson, Karen
E; Schuman, Richard F; Mandy, George T; Stratton, Beth E; Adams,
Karen M; Kramer, William G; Mond, James J
Department of Pediatrics, Baylor College of Medicine, Houston, TX, United
States, [mailto:lweisman@bcm.edu]

International Immunopharmacology, v 9, n 5, p 639-644, May 2009
PUBLICATION DATE: 2009

PUBLISHER: Elsevier Science, P.O. Box 211 Amsterdam 1000 AE Netherlands,
[mailto:nlinfo-f@elsevier.nl], [URL: http://www.elsevier.nl/]

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 1567-5769
FILE SEGMENT: Immunology Abstracts

Safety and pharmacokinetics of a chimerized anti-lipoteichoic acid
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E; Schuman, Richard F; Mandy, George T; Stratton, Beth E; Adams,
Karen M; Kramer, William G; Mond...

ABSTRACT:

A chimerized (murine/human) monoclonal antibody (pagibaximab) against
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DESCRIPTORS: Animal models; Bacteremia; Clinical isolates; Clinical
trials; Data processing; Drugs; Immunoglobulin G; Infection;
Intravenous administration; Lipoteichoic acid; Monoclonal
antibodies; Pharmacokinetics; Risk groups; Statistical analysis;
Staphylococcus aureus; Staphylococcus epidermidis

13/3,K/2 (Item 2 from file: 24)
DIALOG(R) File 24: CSA Life Sciences Abstracts
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0002808824 IP ACCESSION NO: 6495019

Opsonic and protective monoclonal and chimeric antibodies specific for lipoteichoic acid of gram positive bacteria

Fischer, Gerald W Schuman, Richard F; Wong, Hing; Stinson, Jeffrey R

, September 6, 2005
PUBLICATION DATE: 2005

DOCUMENT TYPE: Patent

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

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DESCRIPTORS: Gram positive bacteria; Epitopes; Lipoteichoic acid;
Monoclonal antibodies; Infection; Vaccines; Phagocytosis; Patents

13/3, K/3 (Item 1 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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140058441 CA: 140(5)58441v PATENT

Opsonic monoclonal and chimeric antibodies specific to lipoteichoic acid of Gram positive bacteria for diagnosis and treatment of infection

INVENTOR(AUTHOR): Stinson, Jeffrey R; Schuman, Richard F.; Mond, James J.; Lees, Andrew; Fischer, Gerald Walter

LOCATION: USA

PATENT: U.S. Pat. Appl. Publ.; US 20030235578 A1 DATE: 20031225

APPLICATION: US 323927 (20021220) *US 97055 (19980615) *US PV343503 (20011221)

PAGES: 42 pp., Cont.-in-part of U.S. 6,610,293. CODEN: USXXCO

LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: 424130100; A61K-039/395A; C07K-016/18B

13/3, K/4 (Item 2 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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139116277 CA: 139(8)116277p PATENT

Opsonic monoclonal and chimeric antibodies specific for lipoteichoic acid of Gram-positive bacteria

INVENTOR(AUTHOR): Stinson, Jeffrey R.; Schuman, Richard F.; Mond, James J.; Lees, Andrew; Fischer, Gerald Walter

LOCATION: USA

ASSIGNEE: Biosynexus Incorporated

PATENT: PCT International ; WO 200359260 A2 DATE: 20030724

APPLICATION: WO 2002US41033 (20021223) *US PV343503 (20011221)

PAGES: 99 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: A61K-000/A

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SC; SD; SE; SG; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM. DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

? e au=stinson, jeffrey

Ref	Items	Index-term
E1	1	AU=STINSON, JC
E2	4	AU=STINSON, JE
E3	12	*AU=STINSON, JEFFREY
E4	4	AU=STINSON, JEFFREY A
E5	8	AU=STINSON, JEFFREY A.
E6	2	AU=STINSON, JEFFREY ALAN
E7	1	AU=STINSON, JEFFREY L
E8	3	AU=STINSON, JEFFREY L.
E9	7	AU=STINSON, JEFFREY R
E10	10	AU=STINSON, JEFFREY R.
E11	1	AU=STINSON, JEFFREY RICHARD
E12	1	AU=STINSON, JEFFREY S.

Enter P or PAGE for more

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? s e1-12

>>>Term "12" in invalid position

? s e1-e12

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4	AU=STINSON, JE
12	AU=STINSON, JEFFREY
4	AU=STINSON, JEFFREY A
8	AU=STINSON, JEFFREY A.
2	AU=STINSON, JEFFREY ALAN
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7	AU=STINSON, JEFFREY R
10	AU=STINSON, JEFFREY R.
1	AU=STINSON, JEFFREY RICHARD
1	AU=STINSON, JEFFREY S.

S14 54 E1-E12

? s s14 and (lipoteichoic or teichoic)

54 S14

14841 LI POTEI CHOI C

13613 TEI CHOI C

S15 5 S14 AND (LI POTEI CHOI C OR TEI CHOI C)

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10601171monoclonal.txt
>>>Duplicate detection is not supported for File 393.
>>>Duplicate detection is not supported for File 391.
>>>Records from unsupported files will be retained in the RD set.
S16 4 RD (unique items)
? t s16/3,k/1-4
>>>KWC option is not available in file(s): 399

16/3, K/1 (Item 1 from file: 24)
DIALOG(R) File 24: CSA Life Sciences Abstracts
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0002808824 IP ACCESSION NO: 6495019
Opsonic and protective monoclonal and chimeric antibodies specific for
lipoteichoic acid of gram positive bacteria

Fischer, Gerald W Schuman, Richard F; Wong, Hing; Stinson, Jeffrey
R

, September 6, 2005
PUBLICATION DATE: 2005

DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
FILE SEGMENT: Medical & Pharmaceutical Biotechnology Abstracts

Opsonic and protective monoclonal and chimeric antibodies specific for
lipoteichoic acid of gram positive bacteria

Fischer, Gerald W Schuman, Richard F; Wong, Hing; Stinson, Jeffrey
R

ABSTRACT:

The present invention encompasses monoclonal and chimeric antibodies that
bind to lipoteichoic acid of Gram positive bacteria. The antibodies
also bind to whole bacteria and enhance phagocytosis...

...unknown means to diagnose, prevent and/or treat infections caused by
gram positive bacteria bearing lipoteichoic acid. This invention also
encompasses a peptide mimic of the lipoteichoic acid epitope binding
site defined by the monoclonal antibody. This epitope or epitope peptide
mimic identifies other antibodies that may bind to the lipoteichoic
acid epitope. Moreover, the epitope or epitope peptide mimic provides a
valuable substrate for the...

DESCRIPTORS: Gram positive bacteria; Epitopes; Lipoteichoic acid;
Monoclonal antibodies; Infection; Vaccines; Phagocytosis; Patents

16/3, K/2 (Item 1 from file: 399)
DIALOG(R) File 399: CA SEARCH(R)
(c) 2010 American Chemical Society. All rights reserved.

140058441 CA: 140(5)58441v PATENT
Opsonic monoclonal and chimeric antibodies specific to lipoteichoic acid
of Gram positive bacteria for diagnosis and treatment of infection
INVENTOR(AUTHOR): Stinson, Jeffrey R.; Schuman, Richard F.; Mond, James
J.; Lees, Andrew; Fischer, Gerald Walter
LOCATION: USA

10601171monoclonal.txt

PATENT: U. S. Pat. Appl. Publ. ; US 20030235578 A1 DATE: 20031225
APPLI CATION: US 323927 (20021220) *US 97055 (19980615) *US PV343503
(20011221)

PAGES: 42 pp., Cont.-in-part of U. S. 6,610,293. CODEN: USXXCO

LANGUAGE: English

PATENT CLASSI FICATIONS:

CLASS: 424130100; A61K-039/395A; C07K-016/18B

16/3, K/3 (Item 2 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

(c) 2010 American Chemical Society. All rts. reserv.

139306536 CA: 139(20)306536v PATENT

Production of humanized antibodies by optimizing individual framework regions for diagnostic and therapeutic uses

INVENTOR(AUTHOR): Wong, Hing C.; Stinson, Jeffrey R.; Mosquera, Luis A.

LOCATI ON: USA

ASSI GNEE: Sunol Molecular Corporation

PATENT: U. S. Pat. Appl. Publ. ; US 20030190705 A1 DATE: 20031009

APPLI CATION: US 230880 (20020829) *US PV343306 (20011029) *US 990586

(20011121)

PAGES: 95 pp., Cont.-in-part of U. S. Pat. Appl. 2003 109,680. CODEN:

USXXCO LANGUAGE: English

PATENT CLASSI FICATIONS:

CLASS: 435069100; C12P-021/02A; C12N-005/06B; C07K-016/44B;
C07H-021/04B

16/3, K/4 (Item 3 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

(c) 2010 American Chemical Society. All rts. reserv.

139116277 CA: 139(8)116277p PATENT

Opsonic monoclonal and chimeric antibodies specific for lipoteichoic acid of Gram positive bacteria

INVENTOR(AUTHOR): Stinson, Jeffrey R.; Schuman, Richard F.; Mond, James

J.; Lees, Andrew; Fischer, Gerald Walter

LOCATI ON: USA

ASSI GNEE: Biosynexus Incorporated

PATENT: PCT International ; WO 200359260 A2 DATE: 20030724

APPLI CATION: WO 2002US41033 (20021223) *US PV343503 (20011221)

PAGES: 99 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSI FICATIONS:

CLASS: A61K-000/A

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;
CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH;
GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU;
LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SC; SD;
SE; SG; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM;
ZW AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS
; MW MZ; SD; SL; SZ; TZ; UG; ZM ZW AT; BE; BG; CH; CY; CZ; DE; DK; EE;
ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; SI; SK; TR; BF; BJ; CF; CG;
CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG
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Set	Items	Description
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S5	0	S4 AND (LI POTECHOI C OR TECHOI C)
S6	8	S4 AND (LI POTEI CHOI C OR TEI CHOI C)

S7 6 RD (unique items)
 S8 184 E3- E12
 S9 3 S8 AND (LI POTEI CHOI C OR TEI CHOI C)
 S10 2 RD (unique items)
 S11 38 E3- E9
 S12 6 S11 AND (LI POTEI CHOI C OR TEI CHOI C)
 S13 4 RD (unique items)
 S14 54 E1- E12
 S15 5 S14 AND (LI POTEI CHOI C OR TEI CHOI C)
 S16 4 RD (unique items)

? t s16/3, k/1-4

>>>KW C option is not available in file(s): 399

16/3, K/1 (Item 1 from file: 24)
 DIALOG(R) File 24: CSA Life Sciences Abstracts
 (c) 2010 CSA. All rts. reserv.

0002808824 IP ACCESSION NO: 6495019
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 lipoteichoic acid of gram positive bacteria

Fischer, Gerald W Schuman, Richard F; Wong, Hing; Stinson, Jeffrey
 R

, September 6, 2005
 PUBLICATION DATE: 2005

DOCUMENT TYPE: Patent
 RECORD TYPE: Abstract
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 FILE SEGMENT: Medical & Pharmaceutical Biotechnology Abstracts

Opsonic and protective monoclonal and chimeric antibodies specific for
 lipoteichoic acid of gram positive bacteria

Fischer, Gerald W Schuman, Richard F; Wong, Hing; Stinson, Jeffrey
 R

ABSTRACT:

The present invention encompasses monoclonal and chimeric antibodies that
 bind to lipoteichoic acid of Gram positive bacteria. The antibodies
 also bind to whole bacteria and enhance phagocytosis...

...unknown means to diagnose, prevent and/or treat infections caused by
 gram positive bacteria bearing lipoteichoic acid. This invention also
 encompasses a peptide mimic of the lipoteichoic acid epitope binding
 site defined by the monoclonal antibody. This epitope or epitope peptide
 mimic identifies other antibodies that may bind to the lipoteichoic
 acid epitope. Moreover, the epitope or epitope peptide mimic provides a
 valuable substrate for the...

DESCRIPTORS: Gram positive bacteria; Epitopes; Lipoteichoic acid;
 Monoclonal antibodies; Infection; Vaccines; Phagocytosis; Patents

16/3, K/2 (Item 1 from file: 399)
 DIALOG(R) File 399: CA SEARCH(R)
 (c) 2010 American Chemical Society. All rts. reserv.

140058441 CA: 140(5)58441v PATENT
 Opsonic monoclonal and chimeric antibodies specific to lipoteichoic acid

10601171monoclonal.txt

of Gram positive bacteria for diagnosis and treatment of infection

INVENTOR(AUTHOR): Stinson, Jeffrey R.; Schuman, Richard F.; Mond, James J.; Lees, Andrew; Fischer, Gerald Walter

LOCATION: USA

PATENT: U.S. Pat. Appl. Publ.; US 20030235578 A1 DATE: 20031225

APPLICATION: US 323927 (20021220) *US 97055 (19980615) *US PV343503 (20011221)

PAGES: 42 pp., Cont.-in-part of U.S. 6,610,293. CODEN: USXXCO

LANGUAGE: English

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CLASS: 424130100; A61K-039/395A; C07K-016/18B

16/3, K/3 (Item 2 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

(c) 2010 American Chemical Society. All rights reserved.

139306536 CA: 139(20)306536v PATENT

Production of humanized antibodies by optimizing individual framework regions for diagnostic and therapeutic uses

INVENTOR(AUTHOR): Wong, Hing C.; Stinson, Jeffrey R.; Mosquera, Luis A.

LOCATION: USA

ASSIGNEE: Sunol Molecular Corporation

PATENT: U.S. Pat. Appl. Publ.; US 20030190705 A1 DATE: 20031009

APPLICATION: US 230880 (20020829) *US PV343306 (20011029) *US 990586 (20011121)

PAGES: 95 pp., Cont.-in-part of U.S. Pat. Appl. 2003 109,680. CODEN:

USXXCO LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: 435069100; C12P-021/02A; C12N-005/06B; C07K-016/44B; C07H-021/04B

16/3, K/4 (Item 3 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

(c) 2010 American Chemical Society. All rights reserved.

139116277 CA: 139(8)116277p PATENT

Oposonic monoclonal and chimeric antibodies specific for lipoteichoic acid of Gram positive bacteria

INVENTOR(AUTHOR): Stinson, Jeffrey R.; Schuman, Richard F.; Mond, James J.; Lees, Andrew; Fischer, Gerald Walter

LOCATION: USA

ASSIGNEE: Biosynexus Incorporated

PATENT: PCT International; WO 200359260 A2 DATE: 20030724

APPLICATION: WO 2002US41033 (20021223) *US PV343503 (20011221)

PAGES: 99 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: A61K-000/A

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SC; SD; SE; SG; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM; ZW AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

? s (mono? or antibod? or immunoglobulin) and (lipoteichoic or teichoic)

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Processing

Processed 20 of 56 files ...

Processing

Processed 50 of 56 files ...

Completed processing all files

12202075 MONO?

5873498 ANTI BOD?

1520005 IMMUNOGLOBULIN

14841 LI POTEI CHOI C

13613 TEI CHOI C

S17 7526 (MONO? OR ANTI BOD? OR IMMUNOGLOBULIN) AND (LI POTEI CHOI C OR TEI CHOI C)

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7526 S17

769590 IGG

S18 622 S17 AND IGG

? s s18 and monoclonal

622 S18

1762291 MONOCLONAL

S19 61 S18 AND MONOCLONAL

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>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S20 33 RD (unique items)

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>>>KW C option is not available in file(s): 399

20/3,K/1 (Item 1 from file: 5)

DIALOG(R) File 5: Biosis Previews(R)

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18662668 BIOSIS NO.: 200600008063

Anti-proteinase 3 antibodies (c-ANCA) prime CD14-dependent leukocyte activation

AUTHOR: Hattar Katja; van Buerck Sandra; Bickenbach Annette; Grandel Ulrich; Maus Ulrich; Lohmeyer Juergen; Csernok Elena; Hartung Thomas; Seeger Werner; Grimminger Friedrich; Sibelius Ulf (Reprint)

AUTHOR ADDRESS: Univ Giessen, Dept Internal Med, D-35385 Giessen, Germany** Germany

AUTHOR E-MAIL ADDRESS: ulf.sibelius@inner.med.uni-giessen.de

JOURNAL: Journal of Leukocyte Biology 78 (4): p992-1000 OCT 2005 2005

ISSN: 0741-5400

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Anti-proteinase 3 antibodies (c-ANCA) prime CD14-dependent leukocyte activation

... ABSTRACT: Wegener's granulomatosis (WG), a pathogenetic role has been proposed for circulating anti-neutrophil-cytoplasmic antibodies (ANCA) targeting proteinase 3 (PR3). Disease activation in WG appears to be triggered by bacterial infections. In the present study, we characterized the effect of anti-PR3 antibodies on in vitro activation of isolated monocytes and neutrophils by the bacterial cell-wall components lipopolysaccharide (LPS) and lipoteichoic acid (LTA). Although sole incubation of monocytes and neutrophils with monoclonal anti-PR3 antibodies induced the release of minor quantities of the chemokine interleukin-8 (IL-8), preincubation with anti-PR3 antibodies, but not with isotype-matched control immunoglobulin G (IgG), resulted in a markedly enhanced IL-8

liberation upon LPS challenge. The priming response was...

...TNF- α) and IL-6 synthesis. Comparable priming occurred when leukocytes were preincubated with ANCA-IgG derived from WG serum but not with normal IgG. The priming effect of the anti-PR3 antibody pretreatment was reproduced for LTA challenge of monocytes and neutrophils but not for leukocyte stimulation with TNF- α . Flow cytometric analysis revealed an increase in monocyte and neutrophil membrane CD14 expression during the anti-PR3 priming. We conclude that cytoplasmic ANCA specifically prime CD14-dependent monocytes and neutrophils for activation. The resulting enhanced responsiveness to bacterial pathogens may contribute to the...

...REGISTRY NUMBERS: lipoteichoic acid

DESCRIPTORS:

ORGANISMS: PARTS ETC: monocyte-

CHEMICALS & BIOCHEMICALS: ...monoclonal antibodies; ...

...immunoglobulin G {IgG}; ...

...lipoteichoic acid {LTA}...

...anti-neutrophil cytoplasmic antibodies {ANCA}...

...anti-proteinase 3 antibodies;

20/3, K/2 (Item 2 from file: 5)

DIAGNOSTIC File 5: Biosis Previews(R)

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17135994 BIOSIS NO.: 200300094713

4-1BB (CD137) differentially regulates murine in vivo protein- and polysaccharide-specific immunoglobulin isotype responses to *Streptococcus pneumoniae*.

AUTHOR: Wu Zheng-Q; Khan Abdul Q; Shen Yi; Wolcott Karen M; Dawicki

Wojciech; Watts Tania H; Mittler Robert S; Snapper Clifford M (Reprint)

AUTHOR ADDRESS: Department of Pathology, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Rd., Bethesda, MD, 20814, USA**USA

AUTHOR E-MAIL ADDRESS: csnapper@usuhs.mil

JOURNAL: Infection and Immunity 71 (1): p196-204 January 2003 2003

MEDIUM print

ISSN: 0019-9567 (ISSN print)

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

4-1BB (CD137) differentially regulates murine in vivo protein- and polysaccharide-specific immunoglobulin isotype responses to *Streptococcus pneumoniae*.

...ABSTRACT: an in vivo protein (pneumococcal surface protein A (PspA))- and polysaccharide (phosphorylcholine (PC) determinant of teichoic acid)-specific immunoglobulin (Ig) isotype response to *Streptococcus pneumoniae* was dependent on CD4+ TCR α phbeta+ T cells and B7...

...We demonstrate that mice genetically deficient in 4-1BBL elicit a markedly reduced IgM and IgG anti-PC but normal primary and secondary IgG anti-PspA responses to *S. pneumoniae* relative to those for wild-type mice. However, injection of an agonistic anti-4-1BB monoclonal antibody (MAb), while having no significant effect

on the anti-PC response, strongly inhibits the primary...

DESCRIPTORS:

CHEMICALS & BIOCHEMICALS: ...immunoglobulin M...

...immunoglobulin G...

...anti-4-1BB monoclonal antibody;

20/3, K/3 (Item 3 from file: 5)
 DI ALOG(R) File 5: Biosis Previews(R)
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16086612 BIOSIS NO.: 200100258451

Anti-PR3-antibodies (c-ANCA) prime CD14-dependent monocyte activation

AUTHOR: Hattar Katja (Reprint); von Buerk Sandra (Reprint); Bickenbach Annette (Reprint); Csernok Elena (Reprint); Seeger Werner (Reprint); Grimminger Friedrich (Reprint); Sibelius Ulf (Reprint)

AUTHOR ADDRESS: JLU Giessen, Klinikstrasse 36, Giessen, Hessen, 35392, Germany** Germany

JOURNAL: FASEB Journal 15 (5): pA1065 March 8, 2001 2001

MEDIUM: print

CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001; 20010331

ISSN: 0892-6638

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Abstract

LANGUAGE: English

Anti-PR3-antibodies (c-ANCA) prime CD14-dependent monocyte activation

ABSTRACT: Anti-neutrophil-cytoplasmic-antibodies (c-ANCA) targeting Proteinase-3 (PR3), a serine protease of neutrophils and monocytes, have been implicated in the pathogenesis of systemic vasculitis, such as Wegener's Granulomatosis (WG). While the interaction of anti-PR3-antibodies with neutrophils has been extensively studied in vitro, their effect on inflammatory monocyte behaviour is less well characterized. In the present study, we investigated the influence of monoclonal anti-PR3-antibodies (anti-PR3) and anti-PR3-antibodies from WG-sera (c-ANCA) on cytokine release from highly purified human monocytes. Monocytes were isolated by countercurrent centrifugal elutriation, and secretion products were analyzed by ELISA techniques. PR3 was found to be constitutively expressed on the surface of isolated monocytes in the absence of additional priming procedures. Anti-PR3 challenge per se provoked only the liberation of some minor amounts of IL-8. However, when preincubated with anti-PR3-antibodies, monocyte IL-8 release in response to lipopolysaccharide (LPS)-challenge was massively amplified. This effect was reproduced by c-ANCA originating from WG-sera, whereas human and murine control IgG were ineffective. The anti-PR3-related priming was equally observed when lipoteichoic acid (LTA) from Staph. aureus was employed, but not in response to stimulation with TNF-alpha. Studies with the function-blocking anti-CD14-antibody MY-4 suggested that LPS and LTA-induced monocyte activation were both dependent on CD14, whereas TNF-alpha activated monocytes by a CD14-independent mechanism. Flow cytometry studies revealed a massive upregulation of membrane CD14-expression in response to anti-PR3-treatment. We conclude that anti-PR3-antibodies selectively prime CD14-dependent monocyte activation with upregulation of membrane CD14 as mechanism underlying the priming

10601171monoclonal.txt

response. This anti-PR3-induced enhanced responsiveness of monocytes for activation with bacterial cell wall components such as LPS or LTA may contribute to...

DESCRIPTORS:

ORGANISMS: PARTS ETC: monocyte-

CHEMICALS & BIOCHEMICALS: ... anti-neutrophil-cytoplasmic-antibodies {c-ANCA}...

...lipoteichoic acid

20/3, K/4 (Item 4 from file: 5)
DIALOG(R) File 5: Biosis Previews(R)
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11867838 BIOSIS NO.: 199396032254

Human monoclonal antibody HA-1A binds to endotoxin via an epitope in the lipid A domain of lipopolysaccharide

AUTHOR: Bogard Warren C Jr (Reprint); Siegel Scott A; Leone Ann O; Damiano Evermarie; Shealy David J; Ely Therese M; Frederick Bart; Mascelli Mary A; Siegel Richard C

AUTHOR ADDRESS: Centocor, Inc., 200 Great Valley Parkway, Malvern, PA 19355, USA**USA

JOURNAL: Journal of Immunology 150 (10): p4438-4449 1993

ISSN: 0022-1767

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Human monoclonal antibody HA-1A binds to endotoxin via an epitope in the lipid A domain of lipopolysaccharide

... ABSTRACT: with septic shock, in a controlled clinical trial. To confirm the reported specificity of this antibody for the lipid A domain of endotoxin, several assay systems were developed. These assay systems...

... A prepared from Salmonella minnesota R595 LPS, whereas negative control human IgM mAb or polyclonal antibodies did not. Several experimental approaches were employed to demonstrate the specificity of HA-1A in these assay systems. Both polymyxin B and murine IgG mAb (8A1) with a specificity for lipid A were able to competitively inhibit HA-1A reactivity with lipid A in a dose-dependent manner. Furthermore, a murine IgG anti-Id mAb (9B5.5) developed against HA-1A was also able to block the...

... assessed. Some weak interaction was seen with cardiolipin and chitin, but not with serum proteins, lipoteichoic acid, or DNA.

Collectively, these results conclusively establish that HA-1A binds to the lipid A region of LPS by an interaction with the V region of the antibody.

DESCRIPTORS:

CHEMICALS & BIOCHEMICALS:

MISCELLANEOUS TERMS: ANTIBODY PRODUCTION...

CONCEPT CODES:

20/3, K/5 (Item 5 from file: 5)
DIALOG(R) File 5: Biosis Previews(R)
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09700438 BIOSIS NO.: 198988015553

ANTI-PNEUMOCOCCAL EFFECTS OF C-REACTIVE PROTEIN AND MONOCLONAL

10601171monoclonal.txt

ANTI BODIES TO PNEUMOCOCCAL CELL WALL AND CAPSULAR ANTIGENS
AUTHOR: BRILES D E (Reprint); FORMAN C; HOROWITZ J C; VOLANAKIS J E;
BENJAMIN W H JR; MODANI E L S; ELDRI DGE J; BROOKS J
AUTHOR ADDRESS: DEP PEDIATR, UNI V OF ALA AT BIRMINGHAM, BIRMINGHAM, ALA
35294, USA**USA
JOURNAL: Infection and Immunity 57 (5): p1457-1464 1989
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ANTI PNEUMOCOCCAL EFFECTS OF C-REACTIVE PROTEIN AND MONOCLONAL
ANTI BODIES TO PNEUMOCOCCAL CELL WALL AND CAPSULAR ANTIGENS

ABSTRACT: Antibodies to pneumococcal capsular polysaccharides are well known for their ability to protect against pneumococcal infection. Recent studies indicate that antibodies to cell antigens, including pneumococcal surface protein A and the phosphocholine (PC) determinant of teichoic acids as well as human C-reactive protein (which also binds to PC), can protect...

...and peritoneal cavity. Our findings extend previous results indicating that human C-reactive protein and antibodies to noncapsular antigens are generally less protective than anticapsular antibodies. The new results obtained indicate the following: (i) mouse protection studies with intraperitoneal and intravenous infections provide very similar results; (ii) monoclonal immunoglobulin G2a (IgG2a) antibodies to PC, like IgG1, IgG2b, and IgG3 antibodies to PC, are highly protective against pneumococcal infection in mice; (iii) human antibody to PC is able to protect against pneumococcal infection in mice; (iv) antibodies to PspA are effective at mediating blood and peritoneal clearance of pneumococci; (v) complement is required for the in vivo protective effects of both IgG and IgM antibodies to PC; (vi) IgG1, IgG2b, and IgG3 anti-PC antibodies all mediate complement-dependent lysis of PC-conjugated erythrocytes; and (vii) antibodies and human C-reactive proteins that are reactive with capsular antigens but not cell wall...

20/3, K/6 (Item 6 from file: 5)
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07338477 BIOSIS NO.: 198478073884
SURFACE MARKERS OF HUMAN GINGIVAL FIBROBLASTS IN VITRO CHARACTERIZATION AND
MODULATION BY ENZYMES AND BACTERIAL PRODUCTS
AUTHOR: BARBER S (Reprint); POWELL R N; SEYMOUR G J
AUTHOR ADDRESS: DENTAL SCH, TURBOT ST, BRISBANE 4000, AUSTRALIA**AUSTRALIA
JOURNAL: Journal of Oral Pathology 13 (3): p221-230 1984
ISSN: 0300-9777
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Surface markers of human gingival fibroblasts in vitro were investigated using monoclonal and heterologous antisera against a range of cell surface antigens, together with rosetting techniques, to characterize surface receptors for IgG and [complement] C3. W-38 fibroblasts [embryonic lung] and human peripheral blood monocytes were used as control cells. Human gingival fibroblasts exhibited complement receptors and .beta.a.2-microglobulin...

...DR antigens, and they additionally exhibited a granulocyte antigen not

10601171monoclonal.txt

apparent on W-38 cells. Monolayers of the gingival fibroblasts were further exposed for short periods to varying concentrations of enzymes (trypsin, collagenase and neuraminidase), bacterial extracts (lipopolysaccharide and lipoteichoic acid) and crude supra- and subgingival plaque sonicates. Surface-marker analysis was then carried out...

DESCRIPTORS: HUMAN EMBRYONIC LUNG W-38 CELLS MONOCYTE TRYPSIN COLLAGENASE VI BRIO-CHOLERAEE NEURAMINIDASE PLAQUE SONICATE CELL SURFACE ANTIGEN GRANULOCYTE ANTIGEN IMMUNOGLOBULIN G...

...G-3 SURFACE RECEPTORS HLA-DR ANTIGEN BETA-2 MICRO GLOBULIN LIPO POLY SACCHARIDE LIPO TEICHOIC ACID/

20/3, K/7 (Item 1 from file: 24)
DIALOG(R) File 24: CSA Life Sciences Abstracts
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0003211953 IP ACCESSION NO: 8124962
Peptidoglycan and mannose-based molecular patterns trigger the arachidonic acid cascade in human polymorphonuclear leukocytes

Valera, I; Vigo, AG; Alonso, S; Barboila, L; Crespo, MS; Fernandez, N
Instituto de Biología y Genética Molecular, C/ Sanz y Fores s/n, 47003,
Valladolid, Spain, [mailto:mscres@bgm.uva.es]

Journal of Leukocyte Biology, v 81, n 4, p 925-933, April 1, 2007
PUBLICATION DATE: 2007

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0741-5400
FILE SEGMENT: Immunology Abstracts

ABSTRACT:
... inducers of AA metabolism, as they produced the release of complement-coated zymosan particles and IgG immune complexes. In sharp contrast, lipoteichoic acid, LPS, muramyl dipeptide, and the bacterial lipoprotein mimetic palmitoyl-3-cysteine-serine-lysine-4 failed...

DESCRIPTORS: Abundance; Antigen-antibody complexes; Arachidonic acid; Calpain; Fungi; Immunoglobulin G; Inflammation; Leukocytes; Leukocytes (polymorphonuclear); Leukotriene B4; Lipids; Lipopolysaccharides; Lipoproteins; Lipoteichoic acid; Lipoxigenase; Metabolism; Monoclonal antibodies; Pattern recognition; Phospholipase A2; Prostaglandin E2; Prostaglandin-endoperoxide synthase; Signal transduction; TLR2 protein; Toll-like...

20/3, K/8 (Item 1 from file: 34)
DIALOG(R) File 34: Sci Search(R) Cited Ref Sci
(c) 2010 The Thomson Corp. All rights reserved.

06141338 Genuine Article#: XX775 No. References: 31
Title: Immunopathologic features of Staphylococcus epidermidis-induced endophthalmitis in the rat
Author: Ravindranath RMH (REPRINT); Hasan SA; Mondino BJ
Corporate Source: UNIV SO CALIF, CTR CRANIOFACIAL MOL BIOL, 2250 ALCAZAR ST/LOS ANGELES//CA/ 90033 (REPRINT); UNIV CALIF LOS ANGELES, DORIS STEIN

10601171monoclonal.txt

EYE RES CTR, JULES STEIN EYE INST/LOS ANGELES/ CA/ 90024
Journal: CURRENT EYE RESEARCH, 1997, V16, N10 (OCT), P1036-1043
ISSN: 0271-3683 Publication Date: 19971000
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD, ENGLAND OX2 6DP
Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

... Abstract: saline. The clinical scores, cellular infiltrate in vitreous, and levels of serum and vitreous IgM, IgG and IgA to glycerol teichoic acid (CTA), the major antigenic determinant of S. epidermidis cell wall, were all measured from..

... cells (CD45+/CD3-) was confirmed by flow cytometric analysis of pooled vitreous humor, IgM and IgG but not IgA antibodies to GTA were found in vitreous of injected eyes. The peak of anti-GTA IgM..
... epidermidis-infected rats on day 1 and declined by day 7. In contrast to vitreous antibodies, serum anti-GTA IgM antibodies were significantly elevated throughout the course of S. epidermidis endophthalmitis. A weak IgG but no IgA response were observed in serum. Anti-GTA antibodies were also found in low level in normal sera but not in normal vitreous.

Conclusions. The vitreous antibodies may be involved in neutrophil-mediated opsonophagocytosis leading to 'spontaneous sterility' of the bacteria, and...

... Descriptors: enzyme-linked immunosorbent assay (ELISA); endophthalmitis; IgM antibodies; Staphylococcus epidermidis; vitreous; rat

... Identifiers: AUREUS ENDOPHTHALMITIS; IMMUNE-RESPONSE; RABBIT MODEL; LOCALIZATION; SPECIFICITY; ANTIBODIES; ANTIGEN; EYE

Research Fronts: 95-1513 001 (NATURAL ANTIBODIES; PROTEIN ANTIGENS; IMMUNOMODULATION OF EXPERIMENTAL AUTOIMMUNE MYASTHENIA GRAVIS; MONOCLONAL AUTOANTIBODY; SOMATIC MUTATIONS)

20/3, K/9 (Item 2 from file: 34)
DIALOG(R) File 34: Sci Search(R) Cited Ref Sci
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01067688 Genuine Article#: FT829 No. References: 46
Title: ELISA PROCEDURES FOR THE MEASUREMENT OF IgG SUBCLASS ANTIBODIES TO BACTERIAL-ANTIGENS
Author: RUTHS S; DRIEDIJK PC; WEENING RS; OUTTA
Corporate Source: UNIV AMSTERDAM, ACAD MED CTR, CLIN IMMUNOL LAB, B 1 236, MEI BERGDREEF 9/1105 AZ AMSTERDAM/NETHERLANDS/; UNIV AMSTERDAM, ACAD MED CTR, CLIN IMMUNOL LAB, B 1 236, MEI BERGDREEF 9/1105 AZ AMSTERDAM/NETHERLANDS/; UNIV AMSTERDAM, ACAD MED CTR, DEPT PEDIAT/1105 AZAMSTERDAM/NETHERLANDS/; UNIV AMSTERDAM, ACAD MED CTR, EXPTL & CLIN IMMUNOL LAB CLB/1105 AZ AMSTERDAM/NETHERLANDS/
Journal: JOURNAL OF IMMUNOLOGICAL METHODS, 1991, V140, N1, P67-78
Language: ENGLISH Document Type: ARTICLE (Abstract Available)

Title: ELISA PROCEDURES FOR THE MEASUREMENT OF IgG SUBCLASS ANTIBODIES TO BACTERIAL-ANTIGENS

Abstract: We have developed enzyme-linked immunosorbent assays (ELISA) of IgG subclass antibodies against whole bacteria and bacterial antigens using enzyme-labelled mouse monoclonal antibodies. The properties of different anti-subclass antibodies were compared. In sera from 18 healthy adults we measured the IgG subclass distribution of specific antibodies against Staphylococcus aureus and Haemophilus influenzae b and against distinct bacterial components: pneumococcal capsular polysaccharides, dextran and tetanus toxoid. We found that antibodies against protein (tetanus toxoid) were mainly IgG1, with some contribution of IgG4 and IgG2. Antibodies against

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polysaccharides (pneumococcal PS and dextran) and whole bacteria were restricted mainly to IgG1 and...

... Descriptors: ELISA; IGG SUBCLASS ANTI BODY; MONOCLONAL ANTI BODY; STAPHYLOCOCCUS-AUREUS; HAEMOPHILUS-INFLUENZAE-B; PNEUMOCOCCAL CAPSULAR POLYSACCHARIDE; DEXTRAN; TETANUS TOXOID
... Identifiers: INFLUENZAE TYPE-B; LINKED IMMUNOSORBENT-ASSAY; AUREUS TEICHOIC-ACID; MONOCLONAL-ANTI BODIES; CAPSULAR POLYSACCHARIDE; CHILDRIN; IMMUNOGLOBULIN; DEFICIENCY; AFFINITY; IMMUNIZATION

Research Fronts: 89-0004 003 (IGG SUBCLASSES; PNEUMOCOCCAL ANTI BODIES; EFFECT OF ALLOTYPE G2M(N))
89-2767 001 (RECURRENT ACUTE OTITIS-MEDIA; PENICILLIN TOLERANCE OF...

20/3, K/10 (Item 1 from file: 72)
DI ALOG(R) File 72: EMBASE
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0079011268 EMBASE/Medline No: 2002174964

The utility of IgG subclass measurement for investigating infection-prone patients

Kumararatne D.S.; Joyce H.J.; Jefferis R.

Dept. of Clin. Biochem and Immunol., Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, United Kingdom

CORRESP. AUTHOR/AFFIL: Kumararatne D.S.: Dept. of Clin. Biochem and Immunol., Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, United Kingdom

CORRESP. AUTHOR EMAIL: dsk22@cam.ac.uk

CPD Bulletin Immunology and Allergy (CPD Bull. Immunol. Allergy) (United Kingdom) May 27, 2002, 2/2 (44-47)

CODEN: CBI AF ISSN: 1367-8949

DOCUMENT TYPE: Journal; Review RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

NUMBER OF REFERENCES: 26

The utility of IgG subclass measurement for investigating infection-prone patients

The structure and biological functions of the IgG subclasses are briefly reviewed. The lack of internationally validated reference sera add to the technical...

...which in turn makes it difficult to compare results between different laboratories. The evidence correlating IgG subclass deficiency with susceptibility to infection is weak, leading to a growing scepticism on the use of measuring subclasses when screening for clinically significant immunodeficiency. Measuring specific antibody responses, if necessary after immunisation, is likely to be more useful.

DRUG DESCRIPTORS:

*immunoglobulin class--endogenous compound--ec; *immunoglobulin G--endogenous compound--ec
antibody--endogenous compound--ec; bacterial polysaccharide--endogenous compound--ec; bacterium lipopolysaccharide--endogenous compound--ec; blood clotting factor 8--endogenous compound--ec; dextran--endogenous compound--ec; immunoglobulin A1--endogenous compound--ec; immunoglobulin A2--endogenous compound--ec; immunoglobulin D--endogenous compound--ec; immunoglobulin E--endogenous compound--ec; immunoglobulin G1--endogenous compound--ec; immunoglobulin G2--endogenous compound--ec; immunoglobulin G3--endogenous compound--ec; immunoglobulin G4--endogenous compound--ec; immunoglobulin heavy chain--endogenous compound--ec; immunoglobulin M--endogenous compound--ec; maternal antibody--endogenous compound--ec;

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monoclonal antibody--pharmacology--pd; phospholipase A2
--endogenous compound--ec; Pneumococcus vaccine--drug therapy--dt;
Pneumococcus vaccine--pharmacology--pd; rhesus D antigen--endogenous
compound--ec; teichoic acid--endogenous compound--ec; tetanus toxoid
--endogenous compound--ec

MEDICAL DESCRIPTORS:

antibody response; assay; common variable immunodeficiency;
comparative study; correlation analysis; diagnostic value; disease
predisposition; drug classification; evidence based medicine; Haemophilus
influenzae type b; human; immunization; immunoglobulin G deficiency
--diagnosis--di; immunotherapy; in vitro study; in vivo study; influenza
--drug therapy--dt...

...CAS REGISTRY NO.: 9014-78-2 (dextran); 37341-29-0 (immunoglobulin
E); 97794-27-9 (immunoglobulin G); 9007-85-6 (
immunoglobulin M); 9001-84-7 (phospholipase A2); 9041-38-7 (
teichoic acid); 57425-69-1...

20/3, K/11 (Item 2 from file: 72)
DI ALOG(R) File 72: EMBASE
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0075458827 EMBASE/ Medline No: 1993238383

Isoelectric focusing of immunoglobulins as a new method of immune
response analysis in staphylococcal infections

Tyski S.; Mollby R.; Hryniewicz W

Department of Bacteriology, National Institute of Hygiene, 24 Chocimska,
00-791 Warszawa, Poland

CORRESP. AUTHOR/ AFFIL: Tyski S.: Department of Bacteriology, National
Institute of Hygiene, 24 Chocimska, 00-791 Warszawa, Poland

Serodiagnosis and Immunotherapy in Infectious Disease (SERODIAGN.
IMMUNOTHER. INFECT. DIS.) (United Kingdom) August 30, 1993, 5/2
(109-113)

CODEN: SIIIDE ISSN: 0888-0786

DOI: 10.1016/0888-0786(93)90050-A

DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

The study presents a new way of analysis of IgG response to
staphylococcal antigens. The method is based on the isoelectrofocusing of
human immunoglobulins and after blotting, their reactivity with purified
staphylococcal antigens: alpha-toxin, lipase and teichoic acid. The
method analyses not only total IgG but also the 'monoclonal'
levels of IgG subclasses (clones based on the isoelectric points of
immunoglobulins). When the pattern of IgG response to particular
antigens were compared, a great diversity between patients' sera samples
was observed. The qualitative and quantitative assessment of sera IgG
fractions differentiated by pH gradient revealed the individual character
for each patient. No correlation could be observed between IgG
pattern and the type of staphylococcal infection. Analysing the subclass of
IgG showed that for protein antigens (alphatoxin, lipase) it was
mainly IgG1 but for carbohydrate antigens (teichoic acid) it was
IgG2. No traces of IgG3 and IgG4 fractions were observed.

DRUG DESCRIPTORS:

*immunoglobulin g

MEDICAL DESCRIPTORS:

CAS REGISTRY NO.: 97794-27-9 (immunoglobulin G)

20/3, K/12 (Item 3 from file: 72)
DI ALOG(R) File 72: EMBASE

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0075354178 EMBASE/ Medline No: 1993133720

Human monoclonal antibody HA-1A binds to endotoxin via an epitope in the lipid A domain of lipopolysaccharide

Bogard Jr. W.C.; Siegel S.A.; Leone A.O.; Damiano E.; Shealy D.J.; Ely T.M.; Frederick B.; Mascelli M.A.; Siegel R.C.; Machielse B.; Naveh D.; Kaplan P.M.; Daddona P.E.

Centocor, Inc., 200 Great Valley Parkway, Malvern, PA 19355, United States

CORRESP. AUTHOR/ AFFIL: Bogard Jr. W.C.: Centocor, Inc., 200 Great Valley Parkway, Malvern, PA 19355, United States

Journal of Immunology (J. IMMUNOL.) (United States) May 28, 1993, 150/ 10 (4438-4449)

CODEN: JOIMAH ISSN: 0022-1767

DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

Human monoclonal antibody HA-1A binds to endotoxin via an epitope in the lipid A domain of lipopolysaccharide

...with septic shock, in a controlled clinical trial. To confirm the reported specificity of this antibody for the lipid A domain of endotoxin, several assay systems were developed. These assay systems...

...A prepared from Salmonella minnesota R595 LPS, whereas negative control human IgM mAb or polyclonal antibodies did not. Several experimental approaches were employed to demonstrate the specificity of HA-1A in these assay systems. Both polymyxin B and murine IgG mAb (8A1) with a specificity for lipid A were able to competitively inhibit HA-1A reactivity with lipid A in a dose-dependent manner. Furthermore, a murine IgG anti-IId mAb (9B5.5) developed against HA-1A was also able to block the...

...assessed. Some weak interaction was seen with cardiolipin and chitin, but not with serum proteins, lipoteichoic acid, or DNA. Collectively, these results conclusively establish that HA-1A binds to the lipid A region of LPS by an interaction with the V region of the antibody.

DRUG DESCRIPTORS:

*monoclonal antibody--drug analysis--an; *monoclonal antibody--drug development--dv; *monoclonal antibody--drug dose--do; *monoclonal antibody--pharmacology--pd

MEDICAL DESCRIPTORS:

antibody specificity; antibody structure; article; dose response; enzyme linked immunosorbent assay; gram negative infection; human; human cell; membrane...

20/3, K/13 (Item 1 from file: 73)

DIALOG(R) File 73: EMBASE

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0073234042 EMBASE/ Medline No: 1986088076

ELISA detection of human IgG subclass antibodies to Streptococcus mutans

Challacombe S.J.; Biggerstaff M.; Greenall C.; Kemeny D.M.

Department of Oral Immunology and Microbiology, United Medical and Dental Schools, Guy's Hospital, London SE1 9RT, United Kingdom

CORRESP. AUTHOR/ AFFIL: Department of Oral Immunology and Microbiology, United Medical and Dental Schools, Guy's Hospital, London SE1 9RT, United Kingdom

Journal of Immunological Methods (J. IMMUNOL. METHODS) (Netherlands)

May 7, 1986, 87/1 (95-102)

CODEN: JIMMB ISSN: 0022-1759

DOI: 10.1016/0022-1759(86)90348-0

DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract

LANGUAGE: English

ELISA detection of human IgG subclass antibodies to
Streptococcus mutans

A sensitive enzyme-linked immunosorbent assay (ELISA) has been developed to measure IgG subclass antibodies against whole cells of Streptococcus mutans and to a purified streptococcal antigen (SA 1/II). Bacterial cells were bound to the solid phase using methyl glyoxal and mouse monoclonal antisera against IgG and each IgG subclass were used to detect antibodies. Natural antibodies to S. mutans were predominantly of the IgG1 and IgG2 subclasses, though IgG3 and IgG4 antibodies were detectable in most subjects, and were the majority response in a few subjects. Antibodies to SA 1/II were predominantly of the IgG1 subclass with virtually no activity detectable in the IgG3 and IgG4 subclasses. Inhibition studies suggested some restriction of IgG subclass responses to bacterial antigens since SA 1/II and a polysaccharide could inhibit binding of all subclasses to whole cells of S. mutans equally, whereas glucosyltransferase, lipoteichoic acid and dextran showed greatest inhibition of the IgG3 and IgG4 subclasses.

DRUG DESCRIPTIONS:

*immunoglobulin g; *immunoglobulin subclass

MEDICAL DESCRIPTIONS:

CAS REGISTRY NO.: 97794-27-9 (immunoglobulin G)

20/3, K/14 (Item 2 from file: 73)
DIALOG(R) File 73: EMBASE
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0072730350 EMBASE/Medline No: 1984060766

IgG subclass distribution of antibodies against S. aureus
teichoic acid and alpha-toxin in normal and immunodeficient donors
Hammarstrom L.; Granstrom M.; Oxelius V.; et al
Department of Clinical Immunology, Huddinge University Hospital, S-14186
Huddinge, Sweden:
CORRESP. AUTHOR/ AFFIL: Department of Clinical Immunology, Huddinge
University Hospital, S-14186 Huddinge, Sweden

Clinical and Experimental Immunology (CLIN. EXP. IMMUNOL.) (United
Kingdom) March 30, 1984, 55/3 (593-601)

CODEN: CEXIA ISSN: 0009-9104

DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract

LANGUAGE: English

IgG subclass distribution of antibodies against S. aureus
teichoic acid and alpha-toxin in normal and immunodeficient donors

IgM, IgG, IgA and IgE class and IgG and IgA subclass levels
were determined in 18 IgG2 deficient and six IgG3 deficient donors...
...locus on chromosome 14. IgG3 subclass deficiency was not associated with
further deficiencies. Specific anti-teichoic acid antibodies
were lacking in most IgG2 deficient donors supporting the notion that anti-
teichoic acid antibodies are normally of this subclass. This
was also confirmed in a subclass-specific ELISA using sera from normal
donors although substantial amounts of specific IgG1 antibodies were
also noted. Two IgG2 deficient donors had normal IgG titres (IgG1 in

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the subclass specific ELISA) and the lack of IgG1 anti-teichoic acid antibodies in most IgG2 deficient donors may suggest a lack of maturation of the appropriate idiotype. IgG antibodies to alpha-toxin, a pure protein, were within the lower normal range in a large ...

DRUG DESCRIPTORS:

*alpha toxin; *immunoglobulin G
monoclonal antibody; unclassified drug

MEDICAL DESCRIPTORS:

DRUG TERMS (UNCONTROLLED): teichoic acid antibody

CAS REGISTRY NO.: 97794-27-9 (immunoglobulin G)

20/3, K/15 (Item 1 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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09102492 PMID: 2925841

Extended repertoire of specific antibodies in CSF of patients with subacute sclerosing panencephalitis compared to those with multiple sclerosis: anti-bacterial antibodies are also increased.

Persson M A; Laurenzi M A; Vranjesevic D

Department of Clinical Immunology, Karolinska Institute, Huddinge Hospital, Sweden.

Journal of neuroimmunology (NETHERLANDS) Apr 1989, 22 (2) p135-42,
ISSN 0165-5728--Print Journal Code: 8109498

Publishing Model Print

Document type: Comparative Study; Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Extended repertoire of specific antibodies in CSF of patients with subacute sclerosing panencephalitis compared to those with multiple sclerosis: anti-bacterial antibodies are also increased.

... subacute sclerosing panencephalitis (SSPE), 21 with multiple sclerosis (MS) and 16 controls were analyzed for IgG subclass pattern of anti-viral and anti-bacterial antibodies. In CSF of SSPE and MS patients IgG1 and IgG4 antibodies to measles and IgG1 to mumps were increased compared to the controls. In addition, the SSPE patients had elevated levels of IgG1 to PPD, teichoic acid, and to dextran in CSF. The group of MS patients had decreased levels of IgG1 antibodies to Staphylococcus aureus alpha-toxin.

Descriptors: *Antibodies--cerebrospinal fluid--CF; *Antibodies%%
% Bacterial--analysis--AN; *Multiple Sclerosis--immunology--IM; *Subacute Sclerosing Panencephalitis--immunology--IM; Adolescent; Adult; Aged; Antibodies, Monoclonal--diagnostic use--DU; Antibodies, Monoclonal--immunology--IM; Antibody Specificity; Child; Humans; Immunoglobulin G--analysis--AN; Immunoglobulin G--cerebrospinal fluid--CF; Immunoglobulins--analysis--AN; Middle Aged; Multiple Sclerosis--cerebrospinal fluid--CF; Oligoclonal ...

Chemical Name: Antibodies; Antibodies, Bacterial; Antibodies, Monoclonal; Immunoglobulin G; Immunoglobulins; Oligoclonal Bands

20/3, K/16 (Item 1 from file: 399)
DIALOG(R) File 399: CA SEARCH(R)
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140058441 CA: 140(5) 58441v PATENT

10601171monoclonal.txt

Opsonic monoclonal and chimeric antibodies specific to lipoteichoic acid of Gram positive bacteria for diagnosis and treatment of infection

INVENTOR(AUTHOR): Stinson, Jeffrey R.; Schuman, Richard F.; Mond, James J.; Lees, Andrew; Fischer, Gerald Walter

LOCATION: USA

PATENT: U.S. Pat. Appl. Publ.; US 20030235578 A1 DATE: 20031225

APPLICATION: US 323927 (20021220) *US 97055 (19980615) *US PV343503 (20011221)

PAGES: 42 pp., Cont.-in-part of U.S. 6,610,293. CODEN: USXXCO

LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: 424130100; A61K-039/395A; C07K-016/18B

20/3, K/17 (Item 2 from file: 399)

DI ALOG(R) File 399: CA SEARCH(R)

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130080349 CA: 130(7)80349m PATENT

Opsonic and protective monoclonal and chimeric antibodies specific for lipoteichoic acid of gram positive bacteria

INVENTOR(AUTHOR): Fischer, Gerald W.; Schuman, Richard F.; Wong, Hing; Stinson, Jeffrey L.

LOCATION: USA

ASSIGNEE: Henry M Jackson Foundation for the Advancement of Military Medicine

PATENT: PCT International; WO 9857994 A2 DATE: 19981223

APPLICATION: WO 98US12402 (19980616) *US 49871 (19970616)

PAGES: 150 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: C07K-016/00A

DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; GM; GW; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; UZ; VN; YU; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM. DESIGNATED REGIONAL: GH; GM; KE; LS; MW; SD; SZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG

20/3, K/18 (Item 1 from file: 357)

DI ALOG(R) File 357: Derwent Biotech Res.

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0444208 DBR Accession No.: 2008-02405 PATENT

New pentavalent Staphylococcal antigen composition comprises S. aureus Type 5 antigen, Type 8 antigen, 336 antigen, alpha-toxin antigen, and Staphylococcal leukocidin antigen, for treating methicillin resistant S. aureus infections - immunotherapy method involving preparation of vaccine composition comprising of type 5 antigen, 336 antigen, alpha-toxin antigen and leukocidin antigen-specific monoclonal antibody, useful for the prevention and treatment of methicillin resistant Staphylococcus aureus infection

AUTHOR: TAYLOR K L; FATTOM A I

PATENT ASSIGNEE: NABI BIOPHARMACEUTICALS 2007

PATENT NUMBER: WO 2007145689 PATENT DATE: 20071221 WPI ACCESSION NO.:

2008-B51273 (200810)

PRIORITY APPLIC. NO.: US 875363 APPLIC. DATE: 20061218

NATIONAL APPLIC. NO.: WO 2007US5084 APPLIC. DATE: 20070227

LANGUAGE: English

...composition comprising of type 5 antigen, 336 antigen, alpha-toxin antigen and leukocidin antigen-specific monoclonal antibody

, useful for the prevention and treatment of methicillin resistant Staphylococcus aureus infection

... ABSTRACT: new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are: (1) a method of making a hyperimmune specific intravenous immunoglobulin (IVIg) preparation; (2) a pentavalent Staphylococcal antibody composition comprising (a) a first antibody that specifically binds to a S. aureus Type 5 antigen, (b) a second antibody that specifically binds to a S. aureus Type 8 antigen, (iii) a third antibody that specifically binds to a S. aureus 336 antigen, (iv) a fourth antibody that specifically binds to a S. aureus alpha-toxin antigen, and (v) a fifth antibody that specifically binds to an Staphylococcal leukocidin antigen; (3) a protective antibody composition, comprising (a) a first antibody that specifically binds to an S. aureus alpha-toxin antigen and (b) at least one second antibody that specifically binds to a bacterial antigen other than the S. aureus alpha-toxin antigen...

... comprises one or more additional bacterial antigens selected from S. epidermidis PS1, S. epidermidis GP1, lipoteichoic acid (LTA), and/or microbial surface components recognizing adhesive matrix molecule (MSCRAMM) proteins. Specifically, the...

... toxin antigen is conjugated to at least one of the additional bacterial antigens. In the antibody composition above, at least one of the first through fifth antibodies is a monoclonal antibody or a neutralizing antibody. The fifth antibody specifically binds to a Staphylococcal leukocidin antigen. The protective antibody composition comprises a sub-optimal amount of the first antibody and a sub-optimal amount of the second antibody. It is prepared by (a) administering (i) an S. aureus alpha-toxin antigen and (ii...

... toxin antigen to a human subject, (b) harvesting plasma from the subject, and (c) purifying immunoglobulin from the subject. Preferred Method: Making a hyperimmune specific IVIg preparation comprises administering to a subject the composition, harvesting plasma from the subject, and purifying an immunoglobulin from the subject. Treating or preventing S. aureus infection comprises administering to a subject the...

... administering to a patient the composition comprising (a) a Staphylococcal leukocidin antigen or (b) an antibody that specifically binds to a Staphylococcal leukocidin antigen. Neutralizing Staphylococcal leukocidin infection comprising administering to a patient the composition comprising (a) an S. aureus PVL antigen subunit or (b) an antibody that specifically binds to an S. aureus PVL antigen subunit. ACTIVITY - Antibacterial. Mice that were administered 200 micrograms T5CP specific IgG (AltaStaph IgG) supplemented with 4 mg of alpha-Toxoid derived total rabbit IgG showed 100% protection. The level of protection declined in mice that were immunized with AltaStaph supplemented with either 2 mg or 1 mg toxoid IgG. The survival rate for 2 mg total IgG dose was 90% while for 1 mg dose was 60% after five days of challenge. In contrast, non-supplemented AltaStaph had 30% survival, while no protection observed with toxoid IgG, MEP IgG. MECHANISM OF ACTION - Vaccine. USE - The compositions and methods are useful for treating...

... S. aureus. ADMINISTRATION - Dosage of IVIg composition is 50-1000 mg/kg and dosage of monoclonal antibody composition is 5-25 mg/kg. Administration can be through intramuscular, subcutaneous, intravenous, or intracutaneous...

DESCRIPTORS: type 5 antigen, 336 antigen, alpha-toxin antigen, leukocidin

10601171monoclonal.txt
antigen-specific monoclonal antibody, appl. vaccine,
methicillin resistant Staphylococcus aureus infection prevention,
immunotherapy bacterium therapy (27, 07)
... SECTION: DISEASE-Infectious Disease (non-viral); PHARMACEUTICALS-
Antibodies

20/3, K/19 (Item 2 from file: 357)
DI ALOG(R) File 357: Derwent Biotech Res.
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0324373 DBR Accession No.: 2003-25514 PATENT
Composition comprising monoclonal antibody that specifically
binds to the staphylococcal antigen, useful for blocking and
alleviating staphylococcal nasal colonization - Staphylococcus
aureus-specific chimeric antibody and humanized antibody
production
AUTHOR: KOKAI-KUN J F; MOND J J; FISCHER G W; STINSON J R; WALSH S M;
LEES A
PATENT ASSIGNEE: BIOSYNEXUS INC 2003
PATENT NUMBER: WO 200363772 PATENT DATE: 20030807 WPI ACCESSION NO.:
2003-721613 (200368)
PRIORITY APPLIC. NO.: US 341806 APPLIC. DATE: 20011221
NATIONAL APPLIC. NO.: WO 2002US40925 APPLIC. DATE: 20021223
LANGUAGE: English

Composition comprising monoclonal antibody that specifically
binds to the staphylococcal antigen, useful for blocking and
alleviating staphylococcal nasal colonization - Staphylococcus
aureus-specific chimeric antibody and humanized antibody
production

ABSTRACT: DERWENT ABSTRACT: NOVELTY - A composition (I) comprising at least
one monoclonal antibody (MAb) that specifically binds at
least one antigen of Staphylococci and a mucoadhesive carrier. DETAILED
DESCRIPTION - A composition (I) comprising at least one
monoclonal antibody (MAb) that specifically binds at least
one antigen of Staphylococci and a mucoadhesive carrier. The...

... or 99-110FC12 IE4. The MAb comprises a human heavy chain constant region
chosen from IgG, IgA and IgM, preferably IgG1 human heavy chain
constant region. The MAb comprises a fully...

... scFv. The MAb specifically binds to a staphylococcal surface antigen
(virulence antigens and adherence antigens), lipoteichoic acid
(LTA), or peptidoglycan. (I) comprises a multiplicity of MAbs having
non-identical amino acids...

... colonization. The MAbs work independently of the normal supportive
mechanisms in immune response that enhance antibody activity
against a pathogen. (74 pages)

DESCRIPTORS: Staphylococcus aureus antigen-specific chimeric antibody
, humanized antibody, monoclonal antibody prep.,
liposome, appl. nasal colonization alleviation, bacterium infection
disease therapy bacterium antibacterial antibody engineering
(22, 45)

SECTION: PHARMACEUTICALS-Antibodies-

20/3, K/20 (Item 3 from file: 357)
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0322152 DBR Accession No.: 2003-23292 PATENT
Page 30

Monoclonal antibody with binding specificity for lipoteichoic acid, useful for the treatment of infection caused by gram-positive bacteria e.g. Staphylococcus aureus - for use in Staphylococcus epidermidis and Staphylococcus aureus infection diagnosis and therapy

AUTHOR: STINSON J R; SCHUMAN R F; MOND J J; LEES A; FISCHER G W

PATENT ASSIGNEE: BIOSYNEXUS INC 2003

PATENT NUMBER: WO 200359260 PATENT DATE: 20030724 WPI ACCESSION NO.: 2003-646000 (200361)

PRIORITY APPLIC. NO.: US 343503 APPLIC. DATE: 20011221

NATIONAL APPLIC. NO.: WO 2002US41033 APPLIC. DATE: 20021223

LANGUAGE: English

Monoclonal antibody with binding specificity for lipoteichoic acid, useful for the treatment of infection caused by gram-positive bacteria e.g. Staphylococcus...

ABSTRACT: DERVENT ABSTRACT: NOVELTY - A monoclonal antibody comprising at least one light chain (A1) and at least one heavy chain (B1) binds specifically to lipoteichoic acid (LTA). (A1) and (B1) comprise polypeptides (P1) and (P2) having amino acid sequences with...

...a3) and to heavy chain variable regions (b1), (b2) or (b3) respectively.

DETAILED DESCRIPTION - The monoclonal antibody (MAb) comprising at least one light chain (A1) and at least one heavy chain (B1) binds specifically to lipoteichoic acid (LTA). (A1) and (B1) comprise polypeptides (P1) and (P2) having amino acid sequences with...

...at least one of LTA or a peptide mimotope of LTA that induces anti-LTA antibodies; (b) determining the polypeptide sequence of the light chain variable region of at least one...

... region; and (12) a collection of MAbs that bind to LTA comprising MAbs. BIOTECHNOLOGY - Preferred Antibodies: The amino acid sequence identity of (A1) and (B1) in MAb is at least 80...

... The MAb comprises a heavy chain constant region. The heavy chain constant region comprises human IgG, IgA, IgM or IgD sequence. The MAb comprises a Fab, Fab', F(ab')₂, Fv...

... or as a framework region or its portion respectively. ACTIVITY - Antibacterial. The antibacterial activity of monoclonal antibodies raised in mice against Staphylococcus aureus lipoteichoic acid (LTA). The hybridoma subclone 00-107GG12 ID12 produced IgG-2a monoclonal antibody with a kappa light chain (M120) were tested in an opsonophagocytic assay for opsonic activity...

... with polymorphonuclear neutrophils (PMNs) and complement depleted of anti-S. aureus and anti-S. epidermidis antibodies, and then tested for antibacterial activity against the bacteria. M120 (200 microg/ml) showed opsonic...

... catheters, cardiac valves, cerebrospinal fluid shunts, joint prostheses, other implants). No dosage given. ADVANTAGE - The monoclonal antibodies are broadly reactive and opsonic for Staphylococcus epidermidis and S. aureus. The antibodies bind to the lipoteichoic acid on the bacteria hence prevent the subsequent invasion by the bacteria; enhance bacterial opsonization, phagocytosis and the clearance from the tissue and/or blood. The antibodies are effective against the antibiotic resistant bacteria and eliminate the development of anti-murine antibodies. EXAMPLE - No relevant example given. (48 pages)

DESCRIPTION: monoclonal antibody, humanized antibody prep., isol., expression in hybridoma, appl. Staphylococcus

10601171monoclonal.txt

epidermidis, Staphylococcus aureus infection diagnosis, therapy
antibody engineering cell culture bacterium (22, 40)
SECTION: PHARMACEUTICALS- Antibodies-...

... DIAGNOSTICS- Antibody-Based Diagnostics

20/3, K/21 (Item 4 from file: 357)
DIAGNOSTIC File 357: Derwent Biotech Res.
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0005486 DBR Accession No.: 82-04486
Monoclonal antibodies that specifically recognize the
polyglycerol phosphate backbone and sugar substituents on
lipoteichoic acid (LTA) - hybridoma construction using spleen
cells of mice immunized with killed Streptococcus mutans or Strept.
faecium with myeloma SP2/0 cells and monoclonal antibody
preparation (conference abstract)
AUTHOR: Jackson D; Wong W; Shockman G D
CORPORATE SOURCE: Temple Univ. Sch. Med., Philadelphia, PA, USA.
JOURNAL: Abstr. Annu. Meet. Am Soc. Microbiol. (81 Meet., 144) 1982
CODEN: 0005M
LANGUAGE: English

Monoclonal antibodies that specifically recognize the
polyglycerol phosphate backbone and sugar substituents on
lipoteichoic acid (LTA) ...- mice immunized with killed
Streptococcus mutans or Strept. faecium with myeloma SP2/0 cells and
monoclonal antibody preparation (conference abstract)
... ABSTRACT: fusion with myeloma cell line SP2/0. Doubly cloned cell line
8A1D1A5 produced an IgM monoclonal antibody (Mab) that
agglutinated erythrocytes sensitized with either substituted or
unsubstituted LTAs, at nearly equivalent titres...

... is directed against the polyglycerol phosphate backbone of LTA. Cell
line 6D10G4G6 produced an Mab (IgG) that failed to agglutinate
erythrocytes sensitized with unsubstituted LTA, but agglutinates
erythrocytes sensitized with kojibiose...

DESCRIPTORS: monoclonal antibody prep., lipoteichoic acid
Strept. mutans, Strept. faecium hybridoma construction

20/3, K/22 (Item 1 from file: 457)
DIAGNOSTIC File 457: The Lancet
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0000162020

USE FORMAT 7 OR 9 FOR FULL TEXT

New drugs for exacerbations of chronic obstructive pulmonary disease
Hansel, Trevor T; Barnes, Peter J
The Lancet vol. 374, 9691 PP: 744-55 Aug 29-Sep 4, 2009
DOCUMENT TYPE: PERIODICAL; Feature; Journal Article LANGUAGE: English
RECORD TYPE: New; Fulltext
LENGTH: 12 Pages
WORD COUNT: 8810

TEXT:

... been postulated to be a disease with autoimmune components, 44 such
as circulating pulmonary epithelial IgG autoantibodies⁴⁵ and
anti-elastin autoimmune factors.⁴⁶ Inflammation in COPD might also be
regarded as autoinflammatory... EGF) receptor.^{90,91} Treatment of respiratory
syncytial virus infection remains largely supportive, but the
monoclonal antibody palivizumab against the viral F protein is

licensed for specialist use in restricted circumstances.92...an acute exacerbation might be effective since TNFa concentration increases during exacerbations. However, the TNF antibody infliximab increased the occurrence of respiratory cancers in patients with COPD,125 and increased other...

...TNFa treatment could have substantial implications for other anti-inflammatory treatment for exacerbations of COPD.

Monoclonal antibodies against interleukins 6, 1a, and 17, TGFa, and GM-CSF could be useful for COPD...

...to Pseudomonas endotoxins.129 Hence, tobacco smoke might cause defective anti-bacterial responses. Tocilizumab, a monoclonal antibody that targets interleukin-6 receptors, is effective in several inflammatory diseases,130 but studies in...

SI DEBAR:

CITED REFERENCES:

...31.

71 Hoogerwerf JJ, de Vos AF, Bresser P, et al. Lung inflammation induced by lipoteichoic acid or lipopolysaccharide in humans. Am J Respir Crit Care Med 2008; 178: 34-41...43.

103 Presicce P, Giannelli S, Taddeo A, Villa ML, Della BS. Human defensins activate monocyte-derived dendritic cells, promote the production of proinflammatory cytokines, and up-regulate the surface expression...

THIS IS THE FULL-TEXT.

20/3, K/23 (Item 2 from file: 457)

DI ALOG(R) File 457: The Lancet

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0000153064

USE FORMAT 7 OR 9 FOR FULL TEXT

Neutrophils in development of multiple organ failure in sepsis

Brown, K A; Brain, S D; Pearson, J D; Edgeworth, J D; Et al

The Lancet vol. 368, 9530 PP: 157-69 Jul 8-Jul 14, 2006

DOCUMENT TYPE: PERIODICAL; Feature; Journal Article LANGUAGE: English

RECORD TYPE: New; Fulltext

LENGTH: 13 Pages

WORD COUNT: 12056

TEXT:

...their binding to endothelial cells. From work in our laboratory, which finds that anti-CD11b antibodies are not very effective at inhibiting the interaction of neutrophils from patients with sepsis to endothelial monolayers, it seems that other surface determinants could also contribute to the supranormal adhesiveness of neutrophils in sepsis.32

The beta1 integrins are mainly associated with lymphocytes and monocytes," but one member, VLA-4 (CD49d), was recently identified on approximately 30% of neutrophils from...

...is generally agreed to be due to the activity of circulating factors that include lipopolysaccharide, lipoteichoic acid, and pro-inflammatory cytokines45, 102-105 although binding to endothelium that is activated by...

...the blood concentration of which is frequently increased in sepsis,111 inhibits migration across endothelial monolayers112 whereas the intravenous administration of interleukin 8 to ...the cells.

Neutrophil binding of bacteria is greatly augmented when the pathogens are coated with IgG. The highaffinity receptor for IgG is CD64, which is absent from resting neutrophils and is considered to be a marker

...

...most neutrophils that bind to cultured endothelium, an interaction that is impeded by anti-CD64 antibodies.¹²³ Binding to bacteria also occurs via CD14, the receptor for lipopolysaccharide that is present on all monocytes. This receptor is weakly expressed on neutrophils¹²⁴ but becomes upregulated in response to bacterial infections...

...and CD16 and CD32, which like CD64 also bind the Fc sites (tail regions) of IgG. All of these receptors are adequately expressed on neutrophils from patients with sepsis.

The Toll...

...TLR2(130) and TLR4 agonists could directly delay neutrophil apoptosis, but indirect effects mediated via monocytes and macrophages could be more important for extended neutrophil survival.¹²⁹ Although activation of TLR2...

...implicated in experimentally induced sepsis, but conclusions so far have yet to have clinical effect. Antibodies against TNFalpha and interferon gamma protect baboons¹³⁸ and mice¹³⁹ against bacterial insult, whereas antagonising of... Similar approaches have not been undertaken in the clinical setting but use of anti-CD18 antibodies for patients with traumatic shock¹⁶² or with myocardial infarction¹⁶³ have been disappointing, possibly because of...

...disrupting the adhesion of neutrophils already sequestered in the microvasculature, as shown by anti-integrin antibodies dislodging neutrophils bound to endothelium¹⁶⁵ or the prevention of additional binding interactions that exacerbate...increase the risk of mortality in patients with sepsis. Since polymorphisms in Fc receptors for IgG seem to be associated with meningococcal disease outcome,¹⁶⁸ a similar association might exist between sepsis and CD64, the high-affinity IgG receptor whose expression is upregulated on neutrophils from patients with sepsis⁸⁴ and that is associated...

SI DEBAR:

CAPTIONS:

...eg, interleukin 1, TNFalpha, G-CSF, C5a, nitric oxide) or bacterial products (eg, lipopolysaccharide or lipoteichoic acid), surface integrins and CD64 (high-affinity Fc receptor that binds monomeric IgG) are upregulated to promote firm endothelial adhesion to postcapillary venules. However, some of these factors...

CITED REFERENCES:

...cells in the pathogenesis of vascular damage. In: Cervera R, Khamashta MA, Hughes GRV, eds. Antibodies to endothelial cells and vascular damage. Boca Raton, FL, USA: CRC Press, 1994: 27-46...

...parvulin-primed and lipopolysaccharide-induced hepatic necrosis in rats by selective depletion of neutrophils using monoclonal antibody, J Leukoc Biol 1993; 53: 144-50.

36 Yamano M, Umeda M, Myata K, Yamada... 82 Stubner G, Siedler H. Phagocytosis by neutrophilic granulocytes of intensive care patients: effect of immunoglobulin preparations. Immun Infekt 1984; 12: 69-72.

83 Ahmed NA, McGill S, Yei J, Hu...

... 1984; 160: 1656-71.

99 Daniels RH, Finnen MJ, Hill ME, Lackie JM. Recombinant human monocyte 1L-8 primes NADPH-oxidase and phospholipase A sub 2 activation in human neutrophils. Immunology 74: 64-70.

103 Lotz S, Aga E, Wilde I, et al. Highly purified lipoteichoic acid activates neutrophil granulocytes and delays their spontaneous apoptosis via CD14 and TLR2. J Leukoc...

... 2003; 170: 5268-75.

130 Lotz S, Aga E, Wilde I, et al. Highly purified lipoteichoic acid activates neutrophil granulocytes and delays their spontaneous apoptosis via CD14 and TLR2. J Leukoc... inflammatory responses can be triggered by TRHM 1, a novel receptor expressed on neutrophils and monocytes. J Immunol 2000; 164: 4991-95.

137 Gibot S, Gravoisy AA, Kolopp-Sarda M.N..

... 792-96.

138 Schlag G, Redl H, Davies J, Haller I. Anti-tumour necrosis factor antibody treatment of recurrent bacteremia in a baboon model. Shock 1994; 2: 10-17

139 Doherty...

... 1666-70.

140 Abraham E, Winderink R, Silverman H, et al. Efficacy and safety of monoclonal antibody to human tumour necrosis factor alpha in patients with sepsis syndrome. JAMA 1995; 273: 934-41.

141 Cohen J, Carlet J. INTERSEPT: An international multicentre, placebo-controlled trial of monoclonal antibody to human tumour necrosis factor-alpha in patients with sepsis. International Sepsis Trial Study Group...

20/3, K/24 (Item 3 from file: 457)

DIALOG(R) File 457: The Lancet

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0000152069

USE FORMAT 7 OR 9 FOR FULL TEXT

Laboratory diagnosis of invasive aspergillosis

Hope, W W, Walsh, T J; Denning, D W

The Lancet Infectious Diseases vol. 5, 10 PP: 609-622 Oct 2005

DOCUMENT TYPE: PERIODICAL; General Information LANGUAGE: English

RECORD TYPE: New; Fulltext

LENGTH: 14 Pages

WORD COUNT: 10436

TEXT:

... techniques. The detection of metabolites produced by Aspergillus spp and a range of aspergillus-specific antibodies represent additional, but relatively underused, diagnostic avenues. The detection of galactomannan has been incorporated into immunofluorescence, and in-situ hybridisation

Immunohistochemistry (using the monoclonal antibody WF-AF-117 or EB-A18, 19), immunofluorescence, 20 and in situ hybridisation 21, 22 have been...

... scant, and is likely to remain that way. 38

Galactomannan assays use EB-A2, a monoclonal antibody derived from rats, which is directed towards the B (1,5)-linked galactofuranoside side-chain residues of the galactomannan molecule. 39 Four or more epitopes are required for antibody binding. 3139 Detection is achieved using a sandwich ELISA format, which is made possible by...

... assay is dependent on a pretreatment step, the goal of which is to remove complexing antibody that may block EB-A2 binding. However, the acid-sensitive galactofuranoside residues may be degraded... (1,3)-beta-D glucan results have been documented in haemodialysis, cardiopulmonary bypass, treatment with immunoglobulin products, and exposure to glucan-containing gauze (eg, following major surgery). 69 Environmental (1,3)-beta-D glucan contamination may also compromise specificity.

Antibodies directed toward Aspergillus spp

The demonstration of specific antibody is required to establish the diagnosis of chronic pulmonary aspergillosis.⁶⁹ Traditionally, antibody detection has not been considered useful for the diagnosis of acute invasive aspergillosis, following an early study that failed to document antibody formation in 15 patients with invasive aspergillosis.⁷⁰ Subsequently, antibody has been documented in approximately one-third of patients with invasive aspergillosis.^{47,71} The detection of antibody may prove to be the best non-invasive means of establishing the diagnosis of subacute...

...case report describing invasive pulmonary aspergillosis in an individual with chronic granulomatous disease.⁷² Furthermore, antibody detection could be useful as a means of establishing a retrospective diagnosis of invasive aspergillosis...

...have undergone immunological reconstitution, although more work is required in this regard.

The detection of antibody

Many assay formats have been used to detect antibodies to *Aspergillus* spp, including immunodiffusion, counter immunoelectrophoresis, complement fixation, particle haemagglutination, indirect-immunofluorescence, radioimmunoassay, and ELISA...

SI DEBAR:

...literature using the following terms: "*Aspergillus*", "aspergillosis", "diagnosis", "fungus", "fungal", "culture", "histology", "galactomannan", "glucan", "serology", "antibody", "PCR", "molecular", "metabolite", "mannitol", and "gliotoxin". Further relevant references, not identified by this strategy, were...

CITED REFERENCES:

...Kraft DE. Immunohistologic identification of *Aspergillus* spp. and other hyaline fungi by using polyclonal fluorescent antibodies. *J Clin Microbiol* 1997; 35: 2206-09.

19 Verweij PE, Smeets F, Poot T, Bult... 45 Mennink-Kersten MA, Klint RR, Warris A, Op den Camp HJ, Verweij PE. Bifidobacterium lipoteichoic acid and false ELISA reactivity in aspergillus antigen detection. *Lancet* 2004; 363: 325-27.

46... 37 (suppl 3): S265-80.

70 Young RC, Bennett JE. Invasive aspergillosis. Absence of detectable antibody response. *Am Rev Respir Dis* 1971; 104: 710-16.

71 Chan CM, Woo PC, Leung AS, et al. Detection of antibodies specific to an antigenic cell wall galactomannoprotein for serodiagnosis of *Aspergillus fumigatus* aspergillosis. *J Clin...*

... 2003; 22: 681-85.

73 Kappe R, Schulze-Berge A, Sonntag HG. Evaluation of eight antibody tests and one antigen test for the diagnosis of invasive aspergillosis. *Mycoses* 1996; 39: 13...

...JM, do Carrno JA, Abecasis M, Casimiro C, Exposto F. Follow-up of anti-*Aspergillus* IgG and IgA antibodies in bone marrow transplanted patients with invasive aspergillosis. *J Clin Lab Anal* 2002; 16: 156-62.

76 Holdom MD, Lechenne B, Hay RJ, Hamilton AJ, Monod M. Production and characterization of recombinant *Aspergillus fumigatus* Cu, Zn superoxide, dismutase and its recognition...

THIS IS THE FULL-TEXT.

20/3, K/25 (Item 4 from file: 457)

DIALOG(R) File 457: The Lancet

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USE FORMAT 7 OR 9 FOR FULL TEXT

Radiolabelled antimicrobial peptides for infection detection
Lupetti, Antonella; Velling, Mck M; Pauwels, Ernest K J; Nibbering, Peter H

The Lancet Infectious Diseases vol. 3, 4 PP: 223-229 Apr 2003

DOCUMENT TYPE: PERIODICAL; General Information LANGUAGE: English

RECORD TYPE: New; Fulltext

LENGTH: 7 Pages

WORD COUNT: 5208

TEXT:

... Other agents interact with receptors or domains on infiltrating leucocytes, such as 99mTc-labelled anti-granulocyte monoclonal antibodies (or fragments thereof) and 99mTc-labelled chemotactic peptides and interleukins.⁶ Since antimicrobial peptides often... CD8+ T cells, naive CD4+ T cells, and immature dendritic cells, and beta-defensins recruit monocytes and immature dendritic cells and promote dendritic cell maturation,²⁵ and chemoattract memory T cells...

... negatively charged) surface of microorganisms. Microbial membranes expose negatively charged phospholipids-eg, lipopolysaccharide or teichoic acids-on their surface, while mammalian cells segregate into the inner leaflet the lipids with...

... bacterial surface by esterification of phosphatidylglycerol, the major phospholipid of *Staphylococcus aureus*, or of the teichoic acid polymers.^{33,34} Also, inactivation of antimicrobial peptides by microbial serine proteases as well... g) or large amounts of heat-killed microorganisms. 18 h later 99mTc-peptides or 99mTc-immunoglobulin G (99mTc-IgG), used as a positive tracer for both infection and inflammation, were injected intravenously. Acquisition of...

... muscle in a rat. The quantification of the uptake characteristics of 99mTc-labelled peptides or 99mTc-IgG in infected or inflamed thigh muscles in mice is summarised in figure 4. In agreement...

SI DEBAR:

20/3, K/26 (Item 5 from file: 457)

DI ALOG(R) File 457: The Lancet

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0000145913

USE FORMAT 7 OR 9 FOR FULL TEXT

Molecular basis of group A streptococcal virulence

Bisno, A L; Brito, M O; Collins, C M

The Lancet Infectious Diseases vol. 3, 4 PP: 191-200 Apr 2003

DOCUMENT TYPE: PERIODICAL; General Information LANGUAGE: English

RECORD TYPE: New; Fulltext

LENGTH: 10 Pages

WORD COUNT: 10354

TEXT:

...¹³ The degree of fibrinogen binding, however, varies greatly among different M serotypes.¹⁴

Opsonic antibodies directed against the variable portion of the M-protein molecule override the protective mechanisms described above by activating the classic complement pathway (figure 2). Such antibodies confer type-specific protective immunity. Thus, an individual who acquires antibodies to M type 1 may remain susceptible to other GAS types. Opsonic antibodies do not appear, however, after early and effective antimicrobial therapy.

Recent studies have suggested that...

...duplications of amino acids) in the hypervariable region, which allow these mutant daughter cells to avoid antibody recognition. Presumably, such size mutant bacteria might have a selective survival advantage once herd immunity...

...as members of the emm gene superfamily. A number of the M-like proteins bind IgG or IgA and seem to be cooperative with M protein in antiphagocytic effect. 19, 20...

...that found in human connective tissue. For this reason it is a poor immunogen and antibodies to GAS hyaluronic acid have been quite difficult to demonstrate in people. Such antibodies have, however, been elicited in rabbits immunised with encapsulated GAS31 and in mice immunised with...

...least 17 adhesin candidates have been described, 34 but the most extensively studied have been lipoteichoic acid (LTA), M protein, and fibronectin binding proteins. LTA adheres to fibronectin on human buccal... such entry provides an intraepithelial sanctuary for persistence of the organism sheltered from phagocytes, humoral antibody, and antibiotics such as penicillin that do not readily cross eukaryotic cell membranes. Indeed, there...

...known. Its haemolytic activity is inhibited by serum lipoproteins and other phospholipids. No naturally occurring antibody to it has been detected that will neutralise its haemolytic activity, but synthetic peptides containing amino acid residues of the SLS molecule evoke toxin neutralising antibodies. 76, 77 SLS shares with SLO the capacity to damage the membranes of polymorphonuclear leucocytes... peptidase, which specifically cleaves the human chemotaxin C5a at the PMN binding site. 78, 79 Antibodies to five of the extracellular products have been used in the serodiagnosis of streptococcal infection...

...and generating biologically active peptides such as interleukin-1, 95 kinins, 96 and histamine. 97 Antibodies to SpeB are present in human serum following GAS infection. Studies using genetic mutants clearly...

...proteinases, including C5A peptidase, and streptokinase, have recently been reviewed. 102, 103 Streptolysin O, 104 lipoteichoic acid and peptidoglycan 105 may also stimulate elaboration of cytokines. Only a small fraction of patients...

...to infection outcome are under active investigation. Patients with invasive disease have lower concentrations of antibodies to both M protein and superantigen-neutralising antibodies than do controls. 106 There is a direct correlation between the intensity of inflammatory cytokine... molecules share a particular surface-exposed antigenic domain 133 against which ARF patients mount a strong IgG response. 134 They do not elaborate alpha-lipoproteinase (so-called serum opacity factor) and they... an obvious candidate because of the close association of nephritogenicity and the M serotype. Indeed, monoclonal antibodies raised against human glomeruli have been seen to crossreact with streptococcal M protein. 137 Moreover, in an animal model of nephritis induced by nephritogenic type 12 streptococci, antibodies eluted from the glomerulus were seen to be directed against type 12 M protein but...

...lesions in rhesus monkeys by immunisation with streptococcal membrane fragments or by intravenous injection of antibodies to these fragments. 139 Streptococcal pyrogenic exotoxin B (SpeB, streptococcal proteinase) was identified by immunofluorescence...

...the glomerulus only during the initial phase of APSGN reacts in direct immunofluorescence tests with antibodies present in convalescent sera

of APSGN patients. 141 An apparently identical antigen, found in a...
SI DEBAR:

...related protein (Mrp)
Enn and others
Hyaluronic acid capsule
C5a peptidase
Adherence to epithelial cells
Lipoteichoic acid
(oral epithelial cells)
Fibronectin binding proteins
(oral epithelial cells, cutaneous Langerhans cells)
M protein...

CITED REFERENCES:

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hyaluronic acid by immunization of rabbits with encapsulated streptococci.
J Exp Med 1986; 164...
... hyaluronate in mice: at least two different antigenic sites on
hyaluronate are identified by mouse monoclonal antibodies. J
Exp Med 1988; 168: 971-82.
33 Cunningham MW. Pathogenesis of ... 35 Beachey EH, Simpson WA. The
adherence of group A streptococci to oropharyngeal cells: the
lipoteichoic acid adhesin and fibronectin receptor. Infection 1982;
10: 107-11.
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properties of group A streptococcal lipoteichoic acid. J Exp Med
1975; 187: 1161-67.
37 Dale JB, Baird RW, Courtney HS, Hasty DL, Bronze MS. Passive
protection of mice against group A streptococcal pharyngeal infection by
lipoteichoic acid. J Infect Dis 1994; 169: 319-23.
38 Hasty DL, Ofek I, Courtney HS... bacteria. Cell 2001; 104: 143-52.
76 Dale JB, Chiang EY, Hasty DL, Courtney HS. Antibodies against
a synthetic peptide of SagA neutralize the cytolytic activity of
streptolysin S from group... Stevens DL. Streptococcal toxic shock syndrome:
synthesis of tumor necrosis factor and interleukin-1 by monocytes
stimulated with pyrogenic exotoxin A and streptolysin O. J Infect Dis 1992;
165: 879-85... Proc 1969; 1: 959-63.
137 Goroncy-Bermes P, Dale JB, Beachey EH, Ofek I. W
Monoclonal antibody to human renal glomeruli cross-reacts with
streptococcal M protein. Infect Immun 1987; 55: 2416-19.
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in experimental streptococcal glomerulonephritis. Science 1969; 166:
1032-33.
139 Markowitz AS, Horn D, Aseron...
THIS IS THE FULL-TEXT.

20/3, K/27 (Item 6 from file: 457)
DIALOG(R) File 457: The Lancet
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0000142142

USE FORMAT 7 OR 9 FOR FULL TEXT

Pathogenesis and pathophysiology of pneumococcal meningitis
Koedel, Uwe; Scheld, William Michael; Pfister, Hans-Walter
The Lancet Infectious Diseases vol. 2, 12 PP: 721-736 Dec 2002
DOCUMENT TYPE: PERIODICAL; General Information LANGUAGE: English
RECORD TYPE: New; Fulltext
LENGTH: 16 Pages
WORD COUNT: 13774

TEXT:

... pneumococcus. 49 The IgA1 protease that inactivates the predominant human IgA species by cleaving the immunoglobulin molecule at the heavy-chain hinge region, may allow the pneumococcus to counter the host...

... necessary for bacteriaemic spread. The ability to invade correlates with the presence of the polymeric immunoglobulin receptor (pIgR) on the human cell surface and CbpA on the pneumococcus. The pIgR is important in host defence, transporting antibodies across mucosal epithelial cells. 52 Recent work has shown that, using CbpA that binds directly... of changes in the composition of the capsule and the underlying cell wall components (eg, teichoic acid concentration) rather than in the thickness of the capsule. 57 In addition to the...

... properties, it is capable of activating the classic complement pathway in the absence of specific antibodies, with a concomitant reduction of serum opsonic activity. 62 This activation is mediated by the capacity of pneumolysin to bind the Fc region of IgG 63

The relative contributions of the various putative virulence proteins such as pneumolysin, CbpA, NanA... the primary site of pneumococcal entry into the CSF.

How can a pathogen cross a monolayer of endothelial (or epithelial) cells expressing tight junctions? The pathogen can use several strategies including...

... vacuole and transmigration through the cell. Only transparent pneumococci seem able to transcytose through endothelial monolayers in a significant proportion. 81

The morphological phenotypes termed opaque and transparent because of their...

... interact with the host. 84 In S pneumoniae, the transparent variants produce increased amounts of teichoic acid and CbpA, whereas the opaque variant is associated with larger amounts of capsular polysaccharide...

... to achieve opsonic activity. 85 The concentrations of the other major bacterial opsonin, specific capsular antibody, are also low in normal CSF with a blood/CSF IgG ratio of about 800/1. Although CSF IgG concentrations increase in the presence of bacterial meningitis, they likewise remain below concentrations optimal for...

... susceptibility to invasive disease (versus symptomless nasopharyngeal carriage). These factors include lack of pathogen-specific antibodies, 88 the absence of non-specific opsonins (complement deficiencies; homozygous for mannose-binding lectin codon... Activation of LytA and autolysis results in the release of subcapsular bacterial components including peptidoglycan, lipoteichoic acid, pneumolysin, and bacterial DNA.

Mechanisms of immune activation in bacterial meningitis
Cell-wall products...

... be reproduced by intracisternal challenge with whole, heat-killed unencapsulated strains, their isolated cell walls, lipoteichoic acid, or peptidoglycan, but not by heat-killed encapsulated strains or isolated capsular polysaccharide. 101...

... first step in immune activation is thought to be the binding of peptidoglycan (and/or lipoteichoic acid) to the pattern recognition receptor membrane CD14 (mCD14). 102 However, mCD14 is a glycosyl phosphatidylinositol-linked...

... have substantial immune stimulatory effects on B cells, natural killer (NK) cells, dendritic cells, and monocytes/macrophages. 110, 111 This

activity of bacterial DNA is due to the presence of unmethylated... Spellerberg et al 122 showed that pneumococci activate NF-kappaB in undifferentiated human and mature murine monocytes. The signalling pathways involved in immune activation during acute bacterial meningitis are only just beginning...

...as IL8 and growth-related protein (Gro)alpha are effective chemottractants for neutrophils but not monocytes. By contrast, non-ELR-CXC chemokines (for example, interferon gamma-inducible 10 kDa protein) and CC chemokines (for example, monocyte chemottractant protein (MCP) 1, MIP1alpha, and MIP1beta) are poor chemottractants for neutrophils but attract monocytes and lymphocytes. In human beings, highly raised concentrations of the chemokines IL8, Groalpha, MCP1, MIP1alpha...

...an in-vitro chemotaxis assay, the CSF of bacterial meningitis was chemotactic for neutrophils and mononuclear leucocytes. A significant reduction of neutrophil chemotaxis was obtained by IL8 and Groalpha antibodies, and a reduction of mononuclear-cell migration was achieved by a combination of MCP1, MIP1alpha, and MIP1beta antibodies. 140 In a mouse model of pneumococcal meningitis, the brain mRNA and protein expression of...space. 144 Furthermore, the influx of neutrophils during experimental bacterial meningitis was radically attenuated by antibodies directed against the adhesion molecules Mac1 or ICAM1. 145-147 Both antileucocyte-endothelial interaction strategies...

SI DEBAR:

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148 Nussler...
THIS IS THE FULL-TEXT.

20/3, K/28 (Item 7 from file: 457)
DIALOG(R) File 457: The Lancet
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0000141152

USE FORMAT 7 OR 9 FOR FULL TEXT

Correspondence

Anonymous

The Lancet vol. 360, 9349 PP: 1971 Dec 14, 2002 DOCUMENT TYPE:
PERIODICAL LANGUAGE: English RECORD TYPE: New; Fulltext
LENGTH: 20 Pages
WORD COUNT: 22418

TEXT:

...5 National health policy, policy statement document, final draft.
Afghanistan: Ministry of Public Health, 2002.

Antibody response to Staphylococcal slime and lipoteichoic acid

Sir-Laura Selan and colleagues (June 22, p 2166)¹ describe the exploitation of the antibody response to staphylococcal slime polysaccharide in the diagnosis of vascular graft infection. We have similar experience in measuring the antibody response to exocellular antigens produced by *Staphylococcus epidermidis* and have identified one particular highly immunogenic...

...lipid S.2

This antigen is a short-chain-length exocellular form of the cellular lipoteichoic acid produced by a wide range of gram-positive cocci. We have shown that most of the population have a background serum concentration of IgG directed towards lipid S but that the concentrations rise substantially during serious infection by gram-positive...

...levels to *S. epidermidis* slime antigen were significantly raised compared with those in controls, whereas IgG concentrations were high in patients and controls. The antigen used by Selan and colleagues probably...

...characteristic electrophoretic mobility on SDS-PAGE and can be detected by antisera and commercially-available monoclonal antibodies directed against the glycerolphosphate chain of lipoteichoic acid on western blotting. We have also shown that lipid S can induce the inflammatory response associated with gram-positive sepsis; consequently, neutralisation of antibodies directed towards them could play an important part in lessening the inflammatory response associated with...

...positive infection. There may be a beneficial role for vaccination or passive treatment with such antibodies.⁵

*Tom Elliott, Tony Worthington, Peter Lambert

*Department of Clinical Microbiology, University Hospital, Edgbaston, Birmingham graft infections with antibodies against staphylococcal slime antigens. *Lancet* 2002; 359: 2166-68.

2 Lambert PA, Worthington T, Tebbs...

...potential for detecting infection of grafts. Other workers have emphasised the diagnostic usefulness of the antibody titre for specific bacterial virulence factors.²

We analysed antibody reactivity to *Staphylococcus aureus* recombinant adhesins that recognise matrix molecules in blood collected from convalescent...

...a surface-associated protein capable of binding several extracellular matrix glycoproteins.³

The reactivity of IgG isolated from ten patients with *S. aureus*-induced endocarditis to these proteins was measured by ELISA and compared with the antibody concentrations of five healthy adults or three patients with infective endocarditis caused by unrelated bacterial...

...cut-off, 0.250 optical density (OD) at 490 nm). In patients with staphylococcal endocarditis, antibody concentrations to MAP (≥ 1.6 OD) largely exceeded the cut-off limit, and nine of ten patients exhibited a notable rise in their antibody titre to clumping factor B (≥ 1.2 OD). High IgG reactivity with clumping factor A (≥ 1.5 OD) was seen in six of ten patients, whereas antibody response to fibronectin-binding protein A (≥ 0.8 OD) seemed to be present in all patients.

When the IgG panel was assessed for reactivity to CNA, only two patients were positive with high-titre...

...detectable amounts of cell-wall-associated CNA were seen in only two isolates, perfectly matching IgG antiadhesin profiles.

This finding provides indirect evidence to support the notion that clumping factors and...

...binding protein A are critical factors in inducing *S. aureus* endocarditis and suggests that high IgG titres to MAP, clumping factors A and B, and fibronectin-binding protein A are associated with the disease state and may be useful in identifying staphylococcal endocarditis. No IgG preparation inhibited the binding of fibronectin to isolated fibronectin-binding protein A or to intact...

...1 Selan L, Passariello C, Rizzo L, et al. Diagnosis of vascular graft infections with antibodies against staphylococcal slime antigens. *Lancet* 2002; 359: 2166-68.

2 Colque-Navarro P, Palma M, Soderquist B, Flock J-1, Mollby R. Antibody responses in patients with staphylococcal septicemia against two *Staphylococcus aureus* fibrinogen-binding proteins: clumping factor... the confidentiality of HIV-infected persons.

The blood supply in Singapore undergoes rigorous testing for antibodies to hepatitis B virus, hepatitis C virus, and HIV using the most advanced technology available...

...to developing donor deferral criteria, particularly for HIV-infected donors in preseroconversion windows with negative antibody tests. Indeed, a study involving the Communicable Disease Centre, Singapore General Hospital, and the Singapore...response to this parasite. One study² indicated that this response, and not that of specific antibody, may be central to protecting people when they are first exposed to this parasite. Vaccination...doses, and in four of 650 cancer patients.² Three individuals were found to have antibodies to PEG-rHuMGDF that cross-reacted with endogenous thrombopoietin and neutralised its biological activity. This...

...effect has also been reported in patients treated by erythropoietin who had developed anti-erythropoietin antibodies.³

Patients undergoing the type of treatment Vadhani-Raj and colleagues describe should be screened for antibodies to thrombopoietin to try to better delineate the risks involved in such treatment.

Jean-Luc...

...2 Li J, Yang C, Xia Y, et al. Thrombocytopenia caused by the development of antibodies to thrombopoietin. Blood 2001; 98: 3241-48.

3 Casadevall N, Nataf J, Viron B, et al. Pure red-cell aplasia and antierythropoietin antibodies in patients treated with recombinant erythropoietin. N Engl J Med 2002; 346: 469-75.

Sir... platelet donors. Blood 2001; 98: 1339-45.

Authors' reply

Sir-We are aware that neutralising antibodies resulting in severe thrombocytopenia have been seen in some of the patients and normal donors who received Peg-rHuMGDF. No such neutralising antibodies to recombinant human thrombopoietin were seen in our trial. Moreover, none of the 229 patients...

...For example, female patients with a history of previous pregnancies, if found positive for lymphocytotoxic antibodies, may benefit from autologous donation before administration of intensive chemotherapy. In the TRAP trial, the patients with detectable lymphocytotoxic antibodies did not benefit from leucocyte-reduced or ultraviolet-B-irradiated platelets.4 In our trial...

SI DEBAR:

20/3, K/29 (Item 8 from file: 457)

DI ALOG(R) File 457: The Lancet

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0000101644

USE FORMAT 7 OR 9 FOR FULL TEXT

Rheumatic fever

Gene H Stollerman

The Lancet vol. 349, 9056 PP: 935-42 Mar 29, 1997 DOCUMENT TYPE:

PERIODICAL; Feature; JOURNAL ARTICLE; Journal Article LANGUAGE:

English RECORD TYPE: New; Fulltext

LENGTH: 8 Pages

WORD COUNT: 7069

TEXT:

...it may no longer be possible to detect direct evidence of previous streptococcal infection because antibody titres may have decreased, throat cultures may have become negative, and the minor signs of...

...sign to appear after the antecedent infection with group-A streptococci, can occur when streptococcal antibody concentrations have returned to normal and other evidence of rheumatic inflammation is no longer present...

...of rheumatic fever generally occurs early in the rheumatic attack, at a time when streptococcal antibodies are at their peak concentration, the absence of any substantial increase in the concentrations of these antibodies (eg, antistreptolysin O and anti-DNase B), are useful negative predictors of rheumatic fever. However, when concentrations of such antibodies increase, the diagnosis of rheumatic fever is only presumptive. Increased concentrations of streptococcal antibodies may be caused by a recent coincidental, but unrelated, streptococcal throat infection. The subsequent course... school children with pharyngitis associated with positive cultures for group-A streptococci and with increased streptococcal antibodies, do not develop rheumatic fever. Compared with the patients in military epidemics, these common infections... very short chains in broth cultures. After untreated pharyngitis,

rheumatogenic strains strongly induce type-specific antibodies. Rheumatogenic strains cannot produce lipoprotein lipase, the opacity factor, that is characteristic of skin strains...

...group-A streptococci. 20 Patients with rheumatic fever have higher than normal serum concentrations of IgG directed towards the class-I-specific epitope; such patients also lack immunoreactivity to the class...

...powerful immunising effect. After nasal administration of synthetic M vaccines, mice produce type-specific IgA antibodies and are protected from experimental systemic challenge with homologous M-type strains. 23 The adjuvant... streptococci leaves behind intact fimbriae, by which streptococci adhere to mucosal surfaces. The remaining ligand, lipoteichoic acid, binds to the mucosal receptor, fibronectin. This finding may explain the persistent pharyngeal carriage...

...haptenic carrier, but as a mucosal stimulant for the production of protective IgA type-specific antibodies 23 (figure 4). Several studies already point to the potential of this recombinant protein for oral...
SI DEBAR:

CITED REFERENCES:

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Cunningham MW, Swerlich RA. Polyspecificity of antistreptococcal monoclonal antibodies and their implications in autoimmunity. J Exp Med 1986; 164: 998-1012.
Khanna AK, Buskirk...

...HLA B cell antigen in rheumatic fever patients and their families as defined by a monoclonal antibody. J Clin Invest 1989; 83: 1710-18.

Stollerman GH. Rheumatogenic streptococci and autoimmunity. Clin Immunol...

THIS IS THE FULL-TEXT.

20/3, K/30 (Item 1 from file: 149)
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01307928 SUPPLIER NUMBER: 11461389 (USE FORMAT 7 OR 9 FOR FULL TEXT)

Septic shock: pathogenesis.
Glauser, M.P.; Zanetti, G.; Baumgartner, J.-D.; Cohen, J.
The Lancet, v338, n8769, p732(5)
Sept 21,
1991

PUBLICATION FORMAT: Magazine/Journal ISSN: 0099-5355 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 2658 LINE COUNT: 00287

...ABSTRACT: coagulation pathways may also be activated via mechanisms that are described. When stimulated by LPS, monocytes (the white blood cells that become scavenger cells when they lodge in organs) release cytokines...

... wall components. The classical pathway is mainly activated by complexes of cell-wall components and antibodies. The anaphylatoxins C3a and C5a that result from activation of these pathways are responsible for...

...leucocytes, such as chemotaxis, phagocytosis, and cytotoxicity, (11) and blocking of the adhesion process by monoclonal antibodies prevents tissue injury and improves survival in animal models of septic shock.

Factor XII (Hageman...

...central role in the pathogenesis of septic shock. It is activated by peptidoglycan residues and teichoic acid from the cell wall of gram-positive organisms (*S aureus*, streptococci, pneumococci) as efficiently... of endorphins in the pathophysiology of shock is still incompletely understood. (19)

The cytokine network

Monocytic cells probably have a pivotal role in mediation of the biological effects of LPS (fig...

...remove and detoxify LPS from the blood, thus having a beneficial effect. Second, LPS-stimulated monocytes produce cytokines such as TNF and interleukin 1 (IL-1). Several binding sites for LPS...

...cell surface of macrophage have been described. (20-24) LPS can also interact with the monocytic cell membrane after binding to plasma molecules. An acute-phase protein called LPS-binding protein...

...mortality of LPS. (25) LPS-LBP complexes are a ligand for the CD14 receptors on monocytes and macrophages. (24) LPS when complexed with LBP can stimulate production of TNF by macrophages...

...with shock due to microorganisms that do not contain LPS. In animal models, anti-TNF antibodies given prophylactically before bolus intravenous injections of LPS or gram-negative bacteria, or given therapeutically...

...patterns were to be found during most cases of septic shock in humans, anti-TNF antibodies would be less likely to be effective when administered late in the course of shock...

...shown a pattern of TNF release different from that after bolus inoculation, and anti-TNF antibodies failed to prevent death in these models. [30,31] Thus, the release of TNF in...

...blocking of the binding of IL-1 to its cell-surface receptor, by means of monoclonal antibodies or IL-1 receptor antagonist, prevented the detrimental effects of LPS or *Escherichia coli* inoculation... will help to identify the subsets of patients that might benefit from administration of anticytokine antibodies, and the need for other cytokine inhibitors or anti-inflammatory agents.

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...in rabbits induced by administration of endotoxin or tissue factor: effect of anti-tissue factor antibodies and measurement of plasma extrinsic pathway inhibitor activity. *Blood* 1990; 75: 1481-89.

[15] van... 86.

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DI ALOG(R) File 149: TGG Health & Wellness DB(SM)
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01194382 SUPPLIER NUMBER: 08263509 (USE FORMAT 7 OR 9 FOR FULL TEXT)
 Product information section. (Clinical Laboratory Reference 1989) (buyers
 guide)
 Medical Laboratory Observer, v21, n13, p16(90)
 Annual,
 1989
 DOCUMENT TYPE: buyers guide PUBLICATION FORMAT: Magazine/Journal ISSN:
 0580-7247 LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE:
 Academic; Professional
 WORD COUNT: 57949 LINE COUNT: 05915

... kits for Hepatitis A HAVAB [R] - M El A - Enzyme Immunoassay for the
 detection of IgM antibody to hepatitis A virus. HAVAB
 [R] - M - Radioimmunoassay for the detection of IgM antibody to
 hepatitis A virus. HAVAB [R] El A - Enzyme Immunoassay for the detection of
 antibody to hepatitis A virus. HAVAB [R] -- Radioimmunoassay for the
 detection of antibody to hepatitis A virus.

Diagnostic kits for Hepatitis B AUSAB [R] -- Radioimmunoassay for the
 detection of antibody to hepatitis B surface antigen. AUSAB [R]
 El A - Enzyme Immunoassay for the detection of antibody to hepatitis B
 surface antigen. AUSCELL [R] -- Reverse Passive Hemagglutination for the
 detection of hepatitis...

... surface antigen (HBsAg) in human serum or plasma. Confirmatory test kit
 also available. AUSZYME [R] MONOCLONAL Qualitative third generation
 enzyme immunoassay for the detection of hepatitis B surface antigen (HBsAg)
 in...

... serum or plasma. Confirmatory test kits also available. CORAB
 [R] -- Radioimmunoassay for the detection of antibody to hepatitis B
 core antigen in serum or plasma. CORAB [R] - M Radioimmunoassay for the
 qualitative determination of specific IgM antibody to hepatitis B
 virus core antigen (Anti-[HB.sub.c]IgM) in human serum or...

... 6 months or less) hepatitis B infection. CORZYME [R] -- Enzyme Immunoassay
 for the detection of antibody to hepatitis B core antigen in serum or
 plasma. CORZYME [R] - M Enzyme Immunoassay for the qualitative determination
 of specific IgM antibody to hepatitis B virus core antigen
 (Anti-[HB.sub.c]IgM) in human serum or...

... HBe (rDNA) El A - Enzyme Immunoassay for the detection of hepatitis B e
 antigen and/or antibody to hepatitis B e antigen. ABBOTT-HBe
 (rDNA) -- Radioimmunoassay for the detection of hepatitis B e antigen and/or
 antibody to hepatitis B e antigen.

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 (Human).

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 for the detection of antibody to hepatitis delta antigen (HDAg) in
 human serum or plasma. ABBOTT ANTI-DELTA El A - Enzyme Immunoassay for the
 detection of antibody to hepatitis delta antigen in human serum or
 plasma.

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 serum or plasma. ABBOTT HTLV...

...s). For Research Use Only. ABBOTT HTLV-1 El A - Enzyme Immunoassay for the
 detection of antibodies to human T-Lymphotropic Virus Type 1 (HTLV-1)
 in human serum or plasma.

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...in human fecal specimens. ABBOTT IgE ELA--Enzyme Immunoassay for the quantitative determination of IgE (Immunoglobulin Type E) in human serum or ... plasma. ABBOTT TOXO-G [TM] ELA--Enzyme Immunoassay for the qualitative and quantitative determination of IgG antibody to Toxoplasma gondii in human serum and plasma. ABBOTT TOXO-M [TM] ELA--Enzyme Immunoassay for the qualitative determination of IgM antibody to Toxoplasma gondii in human serum ABBOTT RSV [TM] ELA--Enzyme Immunoassay for the detection...

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... Manual

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...the sample in a reaction cell. During this step, the analyte is captured by the antibody on the microparticle surface. The IMx then adds an alkaline phosphatase conjugate that binds to the analyte/antibody complex on the microparticle surface, forming an antibody /analyte/conjugate "sandwich." The IMx transfers the solution to a glass fiber matrix. The microparticles carrying the conjugate/analyte/antibody "sandwich" adhere to the glass fibers. Excess reagent and other unbound material are washed away...

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(*) Available Summer, 1989

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 Rubella Reference Material.

This reference material provides a precise standard for calibration
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 rubella by hemagglutination inhibition assay, enzyme immunoassay,
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The...

... for Clinical Laboratory Standards (NCCLS) and are traceable to the CDC
 Reference Preparation for Serum Antibody to Rubella. They are
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For In Vitro Diagnostic Use

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T11...

... Msl gG1- FITC Msl gG1- RD1/ Msl gG2a- FITC Msl gM- RD1/ Msl gG1- FITC

Single-Color CYTO-STAT [R]

MONOCLONAL

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PRODUCT

ANTI BODY

DESIGNATION

FORM

For In Vitro Diagnostic Use

T11 (IgG1)

CD2

FITC

RD1

T3 (IgG1)

CD3...

... IgG1)

CD45

FITC

Msl gG1

-

FITC

RD1

Msl gG2a

-

FITC

Msl gG2b

-

FITC

Msl gM

-

FITC

COULTER CLONE [R] MONOCLONAL ANTI BODIES

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PRODUCT

ANTI BODY

DESIGNATION

FORM

For In Vitro Diagnostic Use

T1 (IgG2a)

CD5

Purified

RD1

T3 (IgG1)

CD3...

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 Strep A-CUBE, Mono-CUBE, CMV-CUBE, Rota-CUBE, Rubella-CUBE and
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 bacteria cell wall. This extract is then mixed with specific antibody
 -sensitized latex particles, mixed and read within two minutes.
 There are adequate reagent, extractant, mixing...

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The I CON QSR CKMB assay detects CK-MB in serum by using two different

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* TSH HS

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SERA-TEK Treponemal Antibody Test is designed to be used as an aid in the detection and confirmation of syphilis antibodies.

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Advances in Immunology: The Immune System (First of Two Parts) (Review Article)

Delves, Peter J.; Roitt, Ivan M
The New England Journal of Medicine
Jul 6, 2000; 343 (1), pp 37-49
LINE COUNT: 00712 WORD COUNT: 09832

TEXT

...improve on repeated exposure to a given infection. The innate responses use phagocytic cells (neutrophils, monocytes, and macrophages), cells that release inflammatory mediators (basophils, mast cells, and eosinophils), and natural killer...

...with them in the response to the antigen. B cells secrete immunoglobulins, the antigen-specific antibodies responsible for eliminating extracellular microorganisms. T cells help B cells to make antibody and can also eradicate intracellular pathogens by activating macrophages and by killing virally infected cells...

...from small chemical structures to highly complex molecules. Both the T-cell receptor and the antibody that is embedded in the B-cell membrane, the B-cell receptor, have binding sites... Macrophages (derived from blood-borne monocytes) possess receptors for carbohydrates that are not normally exposed on the cells of vertebrates, (Ref...

...discriminate between ``foreign'' and ``self'' molecules. In addition, both macrophages and neutrophils have receptors for antibodies and complement, so that the coating of microorganisms with antibodies, complement, or both enhances phagocytosis. (Ref. 6) The engulfed microorganisms are subjected to a wide...

...patterns include yeast-cell-wall mannans, lipopolysaccharides on the surface of gram-negative bacteria, and teichoic acids, which are present on gram-positive bacteria. (Ref. 9) |*Figure 1.-Function of Interdigitating... affinity receptors for IgE (Fc(epsilon)R) (Ref. 14) and thereby become coated with IgE antibodies. These cells are important in atopic allergies such as eczema, hay fever, and asthma, in...

...in one of two ways. Like many other cells, they possess Fc receptors that bind IgG (Fc(gamma)R). These receptors link natural killer cells to IgG-coated target cells, which they kill by a process called antibody-dependent cellular cytotoxicity. The second system of recognition that is characteristic of natural killer cells...

...receptors, they play an important part in the clearance of immune complexes consisting of antigen, antibody, and components of the complement system

Soluble Factors in Innate Defense
Innate responses frequently involve...

...triggered by one of three pathways. (Ref. 18) The classic pathway is activated by antigen-antibody complexes, the alternative pathway by microbial-cell walls, and the lectin pathway by the interaction... interferon-(alpha) has proved valuable in the treatment of melanoma. (Ref. 24) Infliximab, a chimeric monoclonal antibody against tumor necrosis factor (alpha), has had strikingly beneficial effects in patients with rheumatoid arthritis...

...become antigen-dependent.

The Structure of Antigen-Specific Molecules The B-Cell Receptor and Soluble Antibodies

Antibodies consist of two identical heavy chains ... and light chains form the constant regions, which define the class and subclass of the antibody and govern whether the light chain is of the (kappa) or (lambda) type. The amino acid sequence of the constant region of the heavy chains specifies five classes of immunoglobulins (IgG, IgA, IgM, IgD, and IgE), four subclasses of IgG, and two subclasses of IgA. These classes and subclasses have different functions. Each type of antibody can be produced as a circulating molecule or as a stationary molecule. The latter type...

...contact with the antigen. One of the two antigen-binding arms (Fab) of the bivalent antibody molecule is indicated. The circulating version of the antibody contains the same four chains but lacks the transmembrane sequence that anchors the B-cell...

...are glycoproteins and contain 3 to 13 percent carbohydrate, depending on the class of the antibody. The carbohydrate is essential in maintaining the structure of the antibody. The basic antibody ``monomeric unit'' (which is biochemically a tetramer) is bivalent, with two antigen-binding arms of identical specificity. Each of these arms can be cleaved proteolytically in the laboratory to yield individual monovalent antigen-binding fragments (Fab) (Fig. 4). (Ref. 30) Another part of the immunoglobulin molecule, the Fc region, contains most of the constant region of the heavy chains. The...

...The T-Cell Receptor

Unlike antibodies, T-cell receptors are produced only as transmembrane molecules. They consist of (alpha)/(beta) or...

...gamma), and (delta) chain contains a variable domain and a constant domain. As in the antibody molecule, the variable domains contain three complementarity-determining regions (Fig. 4), which in the case...

...gamma)/(delta) T cells. Other (gamma)/(delta) T cells do recognize antigen directly, just as antibody molecules do. (Ref. 32)

The Diversity of Antigen Receptors

It has been estimated that lymphocytes are capable of producing about 10^{15} different antibody variable regions (B cells) and a similar number of T-cell-receptor variable regions. Remarkably... TCRA and TCRG loci do not contain D segments. And, as in the case of immunoglobulin genes, each locus contains multiple V, D, and J genes; on TCRA, for example, there...

...joins one gene segment of each type (e.g., VDJC in the case of the immunoglobulin heavy chain) to form a linear coding unit for each chain of the receptor. Each...

...developmental stages of the lymphocyte. The events involved in generating a coding sequence for the immunoglobulin heavy chain are shown. Early in B-cell development, pro-B cells mature into pre...

...genes that do not undergo rearrangement. As the pre-B cell continues to mature, the immunoglobulin light-chain genes undergo rearrangement; the resulting light chain replaces the surrogate light chain, and...

...on the cell surface. The B-cell receptors at this stage also usually include IgD antibodies with the same specificity as the IgM molecule, produced by alternative splicing of the rearranged...

...B cell further differentiates into a plasma cell, which secretes high

levels of the specific antibody (or into a memory B cell). The same general principles regarding the rearrangement process apply... is replaced by another V gene segment. The constant region specifies the class of the antibody (e.g., IgM or IgG), and during the immune response, the VDJ unit in B cells can join with different constant-region genes to alter the class of antibody in a process called class switching. (Ref. 38)

Clonal Selection

There are no more than...

...each B cell is programmed to express only one of the vast number of potential antibodies, all the antigen-receptor molecules on a given lymphocyte have the same specificity. Such clones...

...bind to a unique clone. | *Figure 6.- Recognition of Epitopes by B Cells. Using the antibody molecule as its receptor, the B cell recognizes epitopes on the surface of the antigen...

...is stimulated by this contact, the B cell proliferates, and the resulting clones can secrete antibody whose specificity is the same as that of the cell-surface receptor that bound the...

...within the germinal centers of secondary lymphoid tissues. The changes in amino acids in the antibody that result from this process fine-tune the recognition of antigen by B-cell receptors and determine the strength of binding (affinity) of the antibody. The stronger the binding to antigen, the greater the chance the B cell has of surviving and multiplying -- a classic Darwinian mechanism of selecting cells that produce high-affinity antibodies. The result of clonal selection is a population of B cells with high affinity and...

...immune response, generates both effector T and B cells (cytotoxic and helper T cells and antibody-secreting plasma cells) and memory T and B cells. The memory cells enable a quantitatively...

...larger number of lymphocytes and, in the case of B cells, induces greater levels of antibody that has a greater affinity for the antigen than the antibody of the primary response...

...adhesion and signaling cell-surface molecule. They are the source of the so-called natural antibodies, which are IgM antibodies and are frequently polyreactive (i.e., they recognize several different antigens, often including common pathogens and autoantigens). In most cases, natural antibodies have a relatively low affinity. (Ref. 40, 41...

...to as B2 cells. Before they encounter antigen, mature B2 cells coexpress IgM and IgD antibodies on their cell surface, but by the time they become memory cells, they have usually switched to the use of IgG, IgA, or IgE as their antigen receptors. Complexes of antibodies with a newly encountered antigen and complement are localized in the follicular dendritic cells (a...

...B-cell responses occur. Within these germinal centers, B2 cells that encounter the antigen undergo immunoglobulin class switching and begin to produce IgG, IgA, or IgE, and somatic hypermutation of their antigen-receptor genes occurs. Memory cells and...

...also generated in the germinal centers. The final stages of differentiation of B2 cells into antibody-secreting plasma cells occur within the secondary lymphoid tissues but outside the germinal centers. Although...

...they are subjected to a series of selection procedures (Fig. 7). (Ref.

45) Unlike the antibody molecule, which acts as the antigen receptor on B cells and recognizes antigen in its...

...in immune responses, were originally characterized on the basis of their reactivity to panels of monoclonal antibodies. The antibodies produced by various laboratories were said to form a cluster when they could be grouped... and other infectious organisms. In addition, they have an important immunoregulatory role because they influence antibody production and immunoglobulin class switching by B cells and modify T-cell responses. (Ref. 32) Precisely how they...

...cell population. This is sufficient to maintain tolerance because it denies the help essential for antibody production by self-reactive B cells.

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Response to Oligosaccharide-Protein Conjugate Vaccine against Hemophilus Influenzae b in Two Patients with IgG(sub 2) Deficiency Unresponsive to Capsular Polysaccharide Vaccine (Medical Intelligence)

Insel, Richard A.; , Anderson, Porter W Ph. D.
 The New England Journal of Medicine
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 LINE COUNT: 00386 WORD COUNT: 05335

Response to Oligosaccharide-Protein Conjugate Vaccine against Hemophilus Influenzae b in Two Patients with IgG(sub 2) Deficiency Unresponsive
 Page 67

TEXT

...IN healthy persons IgG antibodies to polysaccharides are predominantly of the IgG(sub 2) subclass (Ref. 1-3). Selective deficiency of this subclass is associated with inability to produce antibodies to bacterial capsular polysaccharides, which confer protective immunity to encapsulated bacteria. However, the basis of the relation between antibody responses to capsular polysaccharide and the IgG(sub 2) subclass has not been defined. Some insight into that mechanism is offered by the present study of two children with selective IgG(sub 2) deficiency and a documented lack of antibody response to immunization with the capsular polysaccharide vaccine of *Hemophilus influenzae* b. Both patients were...

...covalently linked to diphtheria toxoid. In one patient, primary immunization with the conjugate vaccine induced antibody to the capsular polysaccharide and reimmunizations induced anamnestic responses to a moderately high titer (8.4 microgram per milliliter). The induced antibody was predominantly of the IgG(sub 1) subclass, with a contribution from the IgG(sub 2) subclass; it was restricted in diversity and had bactericidal activity in vitro. However, the conjugate vaccine failed to prime for antibody responsiveness to subsequent immunization with the capsular polysaccharide vaccine in this patient, in contrast to healthy young infants, in whom the vaccine both induces antibody and primes for "mature-for-age" responses to the capsular polysaccharide vaccine. In the other patient, primary immunization with conjugate vaccine induced capsular polysaccharide antibody to a titer of 2.1 microgram per milliliter. The antibody was also predominantly of the IgG(sub 1) subclass, included a contribution from the IgG(sub 2) subclass, and had bactericidal activity in vitro. Reimmunization was considered inadvisable. These findings suggest that a defect of immunoregulation was the basis for the antibody unresponsiveness in these patients with IgG(sub 2)-subclass deficiency...

...Serum IgG antibody to diphtheria toxoid was measured by an enzyme-linked immunosorbent assay, and an antibody titer was assigned by comparison with the antibody of a human IgG immunoglobulin preparation that was standardized with reference to the Food and Drug Administration diphtheria horse antitoxin serum (Lot A-43), as previously described (Ref. 5). Total serum antibody to the *H. influenzae* b capsular polysaccharide was estimated in a Farr-type radioantigen binding...

...and calibrated with a standard antiserum from the Office of Biologics (FDA). The distribution of antibody isotypes was determined by an enzyme-linked immunosorbent assay that used wells coated with derived polysaccharide (Ref. 8) and alkaline phosphatase-labeled affinity-purified antibody to human immunoglobulin classes (Tago, Burlingame, Calif.) as the secondary reagents. To determine the IgG subclass of type b capsular polysaccharide antibody, the secondary reagents used were monoclonal antibodies to human IgG subclasses: for IgG(sub 1), BAM15 (Seward Laboratory, Bedford, England); for IgG(sub 2), HP6014; for IgG(sub 3), HP6047; and for IgG(sub 4), HP6022 (Centers for Disease Control, Atlanta). Type-specific monoclonal antibodies were used to determine antibody light chains (HP6053 and HP6054, Centers for Disease Control). Murine monoclonal antibodies were detected by sequential incubation of the wells with a biotinylated goat anti-mouse IgG antibody, which lacked reactivity with human immunoglobulins (Hybridoma Sciences, Atlanta), by incubation with an avidin-biotin...

...The specificity of the IgG subclass-specific monoclonal antibodies has been described (Ref. 9) and was reconfirmed by assay with myeloma proteins and human hybridoma antibodies of the IgG (sub 1) and IgG(sub 2) subclasses ...toxoid, or tetanus toxoid (Ref. 10,11). A difference in titer or affinity of the monoclonal subclass antibody or in the accessibility of the subclass-specific epitopes to binding by monoclonal antibody after the antibody-combining site was occupied by antigen was assayed as described, (Ref. 12) and accounted for less than a twofold difference in the sensitivity in detecting human IgG(sub 1) and IgG(sub 2) subclasses. The murine monoclonal antibody to human IgG(sub 2) was capable of detecting a human hybridoma anticapsular antibody at a level of 1 ng per milliliter...

...Isoelectric focusing analysis of antibody was performed as described elsewhere (Ref. 13). The in vitro bactericidal activity against *H. influenzae*...

...Case Reports

Patient 1

An eight-year-old boy had IgG(sub 2)-subclass deficiency and had had recurrent episodes of otitis media, pneumonia, and formation...

...was no family history of similar symptoms. When the patient was seven years old, the IgG level was 1154 mg per deciliter; IgA, 38 mg per deciliter; IgM, 34 mg per deciliter; IgE, 33 IU per milliliter; IgG (sub 1), 918 mg per deciliter; IgG(sub 2), 20 mg per deciliter (markedly decreased); IgG(sub 3), 57 mg per deciliter; and IgG (sub 4), 63 mg per deciliter (measured by P. Schur, Boston). The isohemagglutinin titer of antibody to blood group A was 1:4, and that to blood group B, 1:2 (both low and delayed in appearance for age); the antibody response to tetanus toxoid immunization was normal; antibody titers were undetectable before immunization with pneumococcal capsular polysaccharide types 1, 4, 6A, 7, 8, 9, 12, and 23, and no antibody response was detected after immunization; antibody titers were detectable but low before immunization with pneumococcal capsular polysaccharide types 3, 14, 18, and 19, and no antibody response was detected after immunizations (performed by G. Schiffman, Brooklyn). The patient had had absolute...

...age of two years.

Patient 2

A 16-year-old girl had combined deficiency of IgG(sub 2), IgG(sub 4), and IgA and had had recurrent otitis media, conjunctivitis, and upper respiratory tract...

...was no family history of similar symptoms. When the patient was 13 years old, the IgG level was 388 mg per deciliter; IgA, 7 mg per deciliter; IgM, 38 mg per deciliter; IgE, 10 IU per milliliter; IgG(sub 1), 270 mg per deciliter; IgG(sub 2), 0; IgG(sub 3), 66 mg per deciliter; and IgG(sub 4), 6 mg per deciliter. The isohemagglutinin titer of antibody to blood group B was 1:2; antibody response to tetanus toxoid immunization was normal; antibody titers were undetectable before immunization with pneumococcal capsular polysaccharide types 3, 4, 6A, 7, 8, 9, 12, and 23, and no antibody response was detected after immunization; antibody titers were low before immunization with types 1, 14, 18, and 19, and no response was detected except a low, nonprotective response to type 18. Antibodies to IgA were detected by passive hemagglutination...

...the patient was 22 months old and again five years later failed to induce an antibody response above the preimmunization titers of 0.02

and 0.04 microgram per milliliter, respectively...

...repeated one and two months later (Table 1). The first of these immunizations increased the antibody titer eightfold, and each of two subsequent booster immunizations also increased the titer. After the three immunizations the final antibody titer (8.4 microgram per milliliter) was approximately 160 times that before immunization (Table 1). Antibody to diphtheria toxoid -- the protein component of the vaccine -- increased to a normal level after...

...vaccine in an attempt to increase the magnitude and prolong the duration of the elevated antibody titer. However, the titer continued to decrease, from 2.5 to 1.8 microgram per...

...and 0.23 microgram per milliliter at 12 months after the third immunization. *Table 1. Antibody Response to Conjugate

(Oligosaccharide-Protein) Vaccine and Polysaccharide Vaccine in Patient 1.

**TABLE OMITTED The isotype of the polysaccharide antibody induced initially by the conjugate vaccine was predominantly IgG (Table 2).

The sixfold increase in antibody titer after the third conjugate-vaccine immunization resulted from contributions of antibody of the IgM as well as the IgG isotype. The decrease in titer three months after the third immunization was accompanied by a decrease of 74 percent in the detected IgM antibody titer and 42 percent in IgG. The IgG subclass of the postimmunization antibody was almost exclusively IgG(sub 1) (Table 3). However, approximately 4 percent of the IgG antibody detected after the third immunization represented IgG(sub 2). No change occurred in the antibody isotype or distribution of IgG subclasses after subsequent reimmunization with the isolated capsular polysaccharide vaccine. *Table 2. Isotype of Antibody to the b Capsular

Polysaccharide Induced by the Conjugate Vaccine in Both Patients *. **TABLE OMITTED *Table 3. IgG Subclass of Antibody to the b Capsular Polysaccharide Induced by the Conjugate Vaccine in Both Patients *. **TABLE OMITTED...

...The antibody induced by conjugate vaccine was almost exclusively of the kappa light-chain type. No antibody was detected in the preimmunization serum by isoelectric focusing analysis (Fig. 1). A single clonotype...

...third immunizations, which also induced new clonotypes. In vitro bactericidal assay of the capsular polysaccharide antibody revealed that the serum titer was less than 2 before the second immunization, 2 after...

...2 at 10 months after the third immunization. *Figure 1. Isoelectric Focusing Patterns of Serum Antibody to the H. influenzae b Capsular Polysaccharide after Immunization with Oligosaccharide-Protein Conjugate Vaccine. Lane...

...G per microgram), cross-linked with 0.1 percent glutaraldehyde, desalted, and dried (Ref. 13). Antibody was detected by exposing the gels to Kodak X-Omat AR film *. **FIGURE OMITTED...

...Patient 2 had no antibody response to immunization with capsular polysaccharide vaccine at 13 or 15 years of age. Immunization with a conjugate vaccine increased the antibody titer 17-fold, to 2.1 microgram per milliliter (Table 4). Local erythema, induration, and tenderness at the site of injection precluded secondary immunization. The induced antibody was mostly IgG, kappa light-chain type, with predominance of the IgG(sub 1) subclass (Tables 2 and 3), and was shown to be restricted by isoelectric focusing analysis. In addition, a distinct, low IgG(sub 2) antibody response was detected after conjugate-vaccine immunization. The vaccine increased bactericidal activity

in serum in...

...preimmunization titer of less than 2 to a titer of 2. *Table 2. Isotype of Antibody to the b Capsular Polysaccharide Induced by the Conjugate Vaccine in Both Patients *. **TABLE OMITTED** *Table 3. IgG Subclass of Antibody to the b Capsular Polysaccharide Induced by the Conjugate Vaccine in Both Patients *. **TABLE OMITTED** *Table 4. Antibody Response to Polysaccharide Vaccine and Conjugate Vaccine in Patient 2. **TABLE OMITTED**

...Discussion

Both patients had deficiency of the IgG(sub 2) subclass, poor antibody responses to the capsular polysaccharide of H. influenzae b and Streptococcus pneumoniae and to blood-group-substance polysaccharides, but normal antibody responses to the protein tetanus toxoid -- an association observed in other patients with the deficiency...

...Immunogenicity of such conjugates may not be assumed to be present in all patients with IgG(sub 2)-subclass deficiency, however, because of the heterogeneity of this disorder (Ref. 15-21...

...The basis of the association between poor capsular-polysaccharide antibody responses and deficiency of the IgG(sub 2) subclass has not been elucidated. IgG(sub 2) deficiency could result from a defect of the IgG(sub 2) heavy-chain constant-region gene or the adjacent switch sequence, as in some patients with IgG(sub 2) deficiency who have a broad gene deletion on chromosome 14 (Ref. 21). Other defects that could cause IgG(sub 2)-subclass deficiency include failure of a T-cell subset to provide -- or of...

...B cell to elicit or respond to -- cellular interactions involved in switching or selecting an IgG(sub 2)-isotype response. In mice, T cells can direct isotype switching (Ref. 22) as well as influence antibody responses to polysaccharides (Ref. 23). In healthy humans the antibody response to a number of bacterial polysaccharides -- levan, dextran, teichoic acids, group A streptococcal polysaccharide, and H. influenzae b and pneumococcal capsular polysaccharide -- is wholly or partly restricted to the IgG(sub 2) subclass (Ref. 1-3, 17, 24, 25). In contrast, IgG(sub 1) and IgG(sub 3) predominate in the human IgG antibody response to protein antigens (Ref. 1, 17, 25). Polysaccharides, with cooperative interactions from T cells, could preferentially activate production of the IgG(sub 2) subclass. A conjugate vaccine would have the potential to bypass poor antibody responses to the unconjugated capsular polysaccharide if the vaccine stimulated cellular interactions for saccharide antibody production as activated by proteins, which act as immunogenic antigens in IgG(sub 2)-subclass deficiency...

...vaccine in these two patients suggests the presence of a defect in cellular cooperation. The immunoglobulin variable-region genes coding for this antibody were not restricted to pairing only with the IgG(sub 2) heavy-chain constant-region gene in these patients. Healthy infants immunized with conjugate vaccines also generate a predominant IgG(sub 1)-subclass antibody response but have a somewhat greater contribution of the IgG(sub 2) isotype to the antibody response than observed here (Ref. 26). The detectable, although low, level of IgG(sub 2) antibody induced by conjugate vaccine in these patients demonstrates that the IgG(sub 2) heavy-chain constant-region gene can be expressed in the antibody response, which makes unlikely a structural defect at the level of the immunoglobulin gene. In addition, the antibody response induced by conjugate vaccine was lower than that observed in healthy older children (Ref. ...

...finding is unknown, but the lower response in our patients was not accompanied by less antibody diversity than in healthy adults or children with conjugate-induced antibody (Ref. 13,27...

...The finding of IgG(sub 1)- and IgG(sub 2)-subclass predominance of antibody after immunization with conjugated (Ref. 26) and unconjugated (Ref. 3,26) forms of the saccharide...

...of the saccharide may activate different cellular interactions. Conjugate vaccines have the ability to induce antibody in healthy infants at an age at which there is a lack of response to...

...5,27-29). Reimmunization of the healthy infant with a conjugate vaccine increases the total antibody titer as well as the IgG titer, with restimulation of B-cell clones that were activated by primary immunization and minimal recruitment of new clones into the expressed-antibody repertoire, (Ref. 27) as was observed in Patient 1. In addition, conjugate vaccines can prime...

...to respond to immunization with unconjugated capsular polysaccharide, which is associated with reactivation of all IgG antibody-secreting clones expressed after conjugate immunization (Ref. 27,28). These observations in healthy children suggest...

...dependent form of the capsular polysaccharide (Ref. 27). The capsular-polysaccharide-induced increase in the antibody titer of normal infants is accompanied by a preferential IgG(sub 2)-subclass antibody response, (Ref. 26) which indicates that the IgG-subclass response of the conjugate-induced memory B cell is dictated by the stimulating form...

...of response to subsequent capsular polysaccharide immunization in Patient 1, with a concomitant increase in antibody titer and IgG(sub 2) antibody production, suggests either an intrinsic defect in the memory B cell generated by the conjugate...

...cooperate with this memory B cell to respond to isolated saccharides and to generate an IgG(sub 2) antibody response. In vitro experiments will be required to delineate the exact cellular basis of this...

...Finally, the antibody titers to the capsular polysaccharide induced by the vaccine were much higher than those considered minimally protective, (Ref. 30) and the antibody induced was shown to have bactericidal activity in vitro. In spite of its decline, the...

...Karen Cerosaletti for technical assistance, to Dr. Charles Reimer (Centers for Disease Control) for the monoclonal antibodies to IgG subclasses, and to Dr. Jose Munoz for critical suggestions.

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Set	Items	Description
S1	99	E26- E31
S2	88	RD (unique items)
S3	0	S2 AND ?TECHOI C?
S4	99	E3- E8
S5	0	S4 AND (LI POTECHOI C OR TECHOI C)
S6	8	S4 AND (LI POTEI CHOI C OR TEI CHOI C)
S7	6	RD (unique items)
S8	184	E3- E12
S9	3	S8 AND (LI POTEI CHOI C OR TEI CHOI C)
S10	2	RD (unique items)
S11	38	E3- E9
S12	6	S11 AND (LI POTEI CHOI C OR TEI CHOI C)
S13	4	RD (unique items)
S14	54	E1- E12
S15	5	S14 AND (LI POTEI CHOI C OR TEI CHOI C)
S16	4	RD (unique items)
S17	7526	(MONO? OR ANTI BOD? OR IMMUNOGLOBULIN) AND (LI POTEI CHOI C OR TEI CHOI C)
S18	622	S17 AND I GG
S19	61	S18 AND MONOCLONAL
S20	33	RD (unique items)